```
=> e paricalcitol/cn
E1            1     PARIC SR/CN
E2            1     PARIC T/CN
E3            1 --> PARICALCITOL/CN
E4            1     PARICIN 13/CN
E5            1     PARICIN 15/CN
E6            1     PARICIN 220/CN
E7            1     PARICIN 285/CN
E8            1     PARICIN 54/CN
E9            1     PARICIN 6/CN
E10           1     PARICIN 9/CN
E11           1     PARICINA/CN
E12           1     PARICINE/CN

=> s e3
L8            1 PARICALCITOL/CN

=> d l8 1

L8   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   131918-61-1  REGISTRY
ED   Entered STN:  08 Feb 1991
CN   19-Nor-9,10-secoergosta-5,7,22-triene-1,3,25-triol,
     (1α,3β,7E,22E)- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   19-Nor-1,25-dihydroxyvitamin D2
CN   Paricalcitol
CN   Zemplar
FS   STEREOSEARCH
DR   539856-25-2
MF   C27 H44 O3
SR   CA
LC   STN Files:   ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CA, CANCERLIT,
       CAPLUS, CIN, DDFU, DIOGENES, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS,
       IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*,
       SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
         (*File contains numerically searchable property data)

Absolute stereochemistry.
Double bond geometry as shown.
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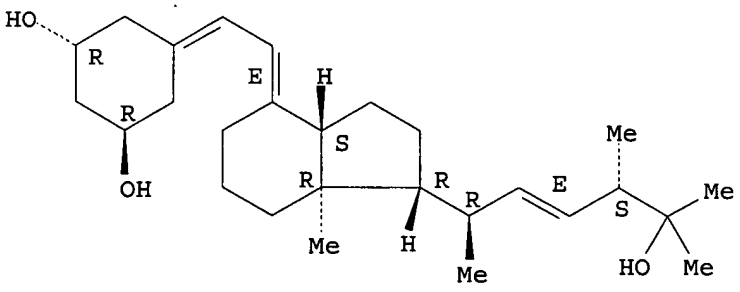


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**
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107 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
107 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file hcaplus

FILE 'REGISTRY' ENTERED AT 01:11:25 ON 02 OCT 2005
E PARICALCITOL/CN
L8 1 S E3

FILE 'HCAPLUS' ENTERED AT 01:17:34 ON 02 OCT 2005

=> s l8 and (cancer? or myelodysplas? or hyperproliferative or hyper(w)proliferative or cancer? or tumour? or tumor? or carcinom? or adenocarcinom? or myelom? or leukem? or neoplas?)
107 L8
270859 CANCER?
2950 MYELODYSPLAS?
1510 HYPERPROLIFERATIVE
14977 HYPER
38339 PROLIFERATIVE
59 HYPER(W)PROLIFERATIVE
270859 CANCER?
3382 TUMOUR?
403913 TUMOR?
141603 CARCINOM?
27549 ADENOCARCINOM?
19464 MYELOM?
97412 LEUKEM?
423929 NEOPLAS?
L9 23 L8 AND (CANCER? OR MYELODYSPLAS? OR HYPERPROLIFERATIVE OR HYPER(W)PROLIFERATIVE OR CANCER? OR TUMOUR? OR TUMOR? OR CARCINOM? OR ADENOCARCINOM? OR MYELOM? OR LEUKEM? OR NEOPLAS?)

=> d l9 abs cbib kwic 1-23

L9 ANSWER 1 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN
AB Recently, the authors reported that a novel, noncalcemic vitamin D analog (19-nor-1,25(OH)2D2; paricalcitol) had anticancer activity. In this study, the authors explored if paricalcitol enhanced anticancer effects of other clin. useful drugs in vitro against a large variety of **cancer** cells. Paricalcitol, when combined with As2O3, showed a markedly enhanced antiproliferative effect against acute myeloid **leukemia** (AML) cells. This combination induced monocytic differentiation of NB-4 acute promyelocytic **leukemia** (APL) cells and HL-60 AML cells and caused both to undergo apoptosis associated with down-regulation of Bcl-2 and Bcl-xL. Paricalcitol induced monocytic differentiation of U937 AML cells, which was partially blocked by inducing expression of APL-related PML-retinoic acid receptor α (RARα) chimeric protein in the U937 cells containing a Zn2+-inducible expression vector coding for this fusion protein (PR9 cells). Exposure to As2O3 decreased levels of PML-RARα in PR9 cells, and the combination of paricalcitol and As2O3 enhanced their monocytic differentiation in parallel with the As2O3-mediated decrease of PML-RARα. Furthermore, As2O3 increased the transcriptional activity of paricalcitol probably by increasing intracellular levels of paricalcitol by decreasing the function of the mitochondrial enzyme 25-hydroxyvitamin D3-24-hydroxylase, which functions to metabolize the active vitamin D in cells. In summary, the combination of paricalcitol and As2O3 potently decreased growth and induced differentiation and apoptosis of AML cells. This probably occurred by As2O3 decreasing levels of both the repressive PML-RARα fusion protein and the vitamin D metabolizing protein, 25-hydroxyvitamin

D3-24-hydroxylase, resulting in increased activity of paricalcitol. The combination of both of these Food and Drug Administration-approved drugs should be considered for treatment of all-trans retinoic acid-resistant APL patients as well as those with other types of AML.

2005:255427 Document Number 142:367012 19-Nor-1,25(OH)2D2 (a novel, noncalcemic vitamin D analogue), combined with arsenic trioxide, has potent antitumor activity against myeloid **leukemia**. Kumagai, Takashi; Shih, Lee-Yung; Hughes, Susan V.; Desmond, Julian C.; O'Kelly, James; Hewison, Martin; Koeffler, H. Phillip (Division of Hematology/Oncology, Cedars-Sinai Medical Center, University of California at Los Angeles School of Medicine, Los Angeles, CA, 90048, USA). Cancer Research, 65(6), 2488-2497 (English) 2005. CODEN: CNREA8. ISSN: 0008-5472. Publisher: American Association for Cancer Research.

TI 19-Nor-1,25(OH)2D2 (a novel, noncalcemic vitamin D analogue), combined with arsenic trioxide, has potent antitumor activity against myeloid **leukemia**

AB . . . the authors explored if paricalcitol enhanced anticancer effects of other clin. useful drugs in vitro against a large variety of **cancer** cells. Paricalcitol, when combined with As2O3, showed a markedly enhanced antiproliferative effect against acute myeloid **leukemia** (AML) cells. This combination induced monocytic differentiation of NB-4 acute promyelocytic **leukemia** (APL) cells and HL-60 AML cells and caused both to undergo apoptosis associated with down-regulation of Bcl-2 and Bcl-xL. Paricalcitol. . .

ST paricalcitol arsenic trioxide antitumor myeloid **leukemia**

IT Antitumor agents
Apoptosis
Combination chemotherapy
Human
(19-nor-1,25(OH)2D2 (a novel, noncalcemic vitamin D analog), combined with arsenic trioxide, has potent antitumor activity against myeloid **leukemia**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bcl-2; 19-nor-1,25(OH)2D2 (a novel, noncalcemic vitamin D analog), combined with arsenic trioxide, has potent antitumor activity against myeloid **leukemia**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bcl-xL; 19-nor-1,25(OH)2D2 (a novel, noncalcemic vitamin D analog), combined with arsenic trioxide, has potent antitumor activity against myeloid **leukemia**)

IT Fusion proteins (chimeric proteins)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PML-RAR-α; 19-nor-1,25(OH)2D2 (a novel, noncalcemic vitamin D analog), combined with arsenic trioxide, has potent antitumor activity against myeloid **leukemia**)

IT **Leukemia**
(acute promyelocytic; 19-nor-1,25(OH)2D2 (a novel, noncalcemic vitamin D analog), combined with arsenic trioxide, has potent antitumor activity against myeloid **leukemia**)

IT **Leukemia**
(myelogenous; 19-nor-1,25(OH)2D2 (a novel, noncalcemic vitamin D analog), combined with arsenic trioxide, has potent antitumor activity against myeloid **leukemia**)

IT 53112-53-1, 25-Hydroxyvitamin D3-24-hydroxylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(19-nor-1,25(OH)2D2 (a novel, noncalcemic vitamin D analog), combined with arsenic trioxide, has potent antitumor activity against myeloid **leukemia**)

IT 50-02-2, Dexamethasone 1327-53-3, Arsenic trioxide **131918-61-1**, Paricalcitol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(19-nor-1,25(OH)2D2 (a novel, noncalcemic vitamin D analog), combined with arsenic trioxide, has potent antitumor activity against myeloid **leukemia**)

L9 ANSWER 2 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB The invention relates to novel methods and kits for monitoring the therapeutic inactivating capacity of a subject. The invention further relates to methods and kits for determining and/or monitoring a therapeutic protocol for a subject afflicted with auto-antibodies specific for a natural substance, wherein these auto antibodies develop as a result of therapeutic administration of the natural substance or an analog thereof. These methods and kits can be used, for example, to initiate, terminate, or adjust the level of administration of any of a variety of therapeutic agents.

2005:238545 Document Number 142:291446 Methods and kits for monitoring resistance to therapeutic agents. Cantor, Thomas L. (USA). U.S. Pat. Appl. Publ. US 2005059023 A1 20050317, 24 pp. (English). CODEN: USXXCO. APPLICATION: US 2003-664263 20030916.

IT AIDS (disease)
Aerosols
Allergy
Allergy inhibitors
Alzheimer's disease
Analgesics
Anti-AIDS agents
Anti-Alzheimer's agents
Anti-infective agents
Anti-inflammatory agents
Anti-ischemic agents
Antiarthritics
Antiasthmatics
Antidiabetic agents
Antimicrobial agents
Antimigraine agents
Antiparkinsonian agents
Antipyretics
Antitumor agents
Antiviral agents
Arthritis
Asthma
Blood, disease
Cardiovascular agents
Cardiovascular system, disease
Cytoprotective agents
Cytotoxicity
Diabetes mellitus
Digestive tract, disease
Disease, animal
Drug resistance
Ear, disease

Electron-hole plasma
Endocrine system, disease
Eye, disease
Eye, disease
Fever and Hyperthermia
Gout
Human
Human immunodeficiency virus
Immunity
Immunomodulators
Infection
Inflammation
Kidney, disease
Liver, disease
Mental disorder
Musculoskeletal diseases
Neoplasm
Nervous system, disease
Nervous system agents
Nose, disease
Osteoporosis
Pain
Parasiticides
Parathyroid gland, disease
Parkinson's disease
Pharynx, disease
Psychotropics
Respiratory tract, disease
Sexually transmitted diseases
Signal transduction, biological
Skin preparations (pharmaceutical)
Urinary tract, disease
Uterus, disease
(methods and kits for monitoring resistance to therapeutic agents)

IT 50-28-2, ESTRADIOL, biological studies 50-48-6, Amitriptyline 50-78-2, ASPIRIN 51-48-9, Levothyroxine, biological studies 51-57-0, Adipex 52-01-7, SPIRONOLACTONE 52-53-9, Verapamil 53-03-2, PREDNISONE 54-31-9, LASIX 55-03-8, SYNTHROID 57-41-0, Phenytoin 58-93-5, HYDROCHLOROTHIAZIDE 59-30-3, FOLIC ACID, biological studies 60-54-8, TETRACYCLINE 60-87-7, PROMETHAZINE 67-20-9, MACROBID 68-88-2, Hydroxyzine 72-69-5, NORTRIPTYLINE 76-42-6, Oxycodone 78-44-4, SOMA 81-81-2, Warfarin 83-43-2, METHYLPREDNISOLONE 122-09-8, Phentermine 124-90-3, OXYCONTIN 129-06-6, COUMADIN 132-98-9, PENICILLIN VK 152-11-4, Verapamil hydrochloride 300-62-9, Adderall 300-62-9D, Amphetamine, compds. 303-53-7, CYCLOBENZAPRINE 315-30-0, Allopurinol 364-62-5, METOCLOPRAMIDE 439-14-5, DIAZEPAM 443-48-1, METRONIDAZOLE 520-85-4, MEDROXYPROGESTERONE 525-66-6, PROPRANOLOL 564-25-0, Doxycycline 569-65-3, MECLIZINE 630-93-3, DILANTIN 657-24-9, Metformin 846-49-1, LORAZEPAM 846-50-4, TEMAZEPAM 1400-61-9, Nystatin 1622-61-3, CLONAZEPAM 1665-48-1, SKELAXIN 4205-90-7, CLONIDINE 8015-29-0, ORTHONOVUM 10118-90-8, MINOCYCLINE 10238-21-8, GLYBURIDE 10540-29-1, TAMOXIFEN 11096-26-7, Erythropoietin 12650-69-0, BACTROBAN 14124-50-6 15307-86-5, DICLOFENAC 15686-71-2, CEPHALEXIN 15687-27-1, IBUPROFEN 18323-44-9, CLINDAMYCIN 18559-94-9, Albuterol 19794-93-5, TRAZODONE 21829-25-4, NIFEDIPINE 22204-53-1, NAPROXEN 24390-14-5, DOXYCYCLINE HYCLATE 26787-78-0, Amoxicillin 26921-17-5, TIMOLOL MALEATE 27203-92-5, TRAMADOL 28981-97-7,

Alprazolam 29122-68-7, ATENOLOL 36282-47-0, ULTRAM 36505-84-7, BUSPIRONE 49562-28-9, TRICOR 51022-70-9, Albuterol sulfate 51333-22-3, RHINOCORT AQUA 51384-51-1, Metoprolol 52232-67-4, FORTEO 54910-89-3, FLUOXETINE 56392-17-7, METOPROLOL TARTRATE 57308-51-7 59277-89-3, Acyclovir 59729-32-7, CELEXA 59729-33-8, Citalopram 60142-96-3, NEURONTIN 62571-86-2, CAPTOPRIL 63590-64-7, TERAZOSIN 66357-35-5, Ranitidine 66357-59-3, Ranitidine hydrochloride 66376-36-1, Alendronate 72956-09-3, COREG 73590-58-6, PRILOSEC 74191-85-8, DOXAZOSIN 74469-00-4, Augmentin ES 600 75847-73-3, ENALAPRIL 76547-98-3, LISINOPRIL 76584-70-8, DEPAKOTE 76824-35-6, FAMOTIDINE 78246-49-8, SEROXAT 79198-29-1 79559-97-0, ZOLOFT 79617-96-2, Sertraline 79794-75-5, CLARITIN 79902-63-9, ZOCOR 80474-14-2, FLOVENT 81093-37-0, Pravastatin 81131-70-6, PRAVACHOL 82586-55-8, Accupril 82626-48-0, Zolpidem 82640-04-8, EVISTA 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 83881-52-1, ZYRTEC 83905-01-5, ZITHROMAX 83919-23-7, NASONEX 84449-90-1, Raloxifene 85441-61-8, Quinapril 85650-52-8, REMERON 85721-33-1, Ciprofloxacin 86386-73-4, DIFLUCAN 86541-74-4, LOTENSIN 86541-75-5, Benazepril 87333-19-5, Altace 88889-14-9, MONOPRIL 89365-50-4, Salmeterol 90566-53-3, Fluticasone 92665-29-7, CEFZIL 93107-08-5, CIPRO 93479-97-1, Amaryl 94749-08-3, SEREVENT 97240-79-4, TOPAMAX 98048-97-6, Fosinopril 98418-47-4, TOPROLXL 99294-93-6, Ambien 100643-71-8, CLARINEX 100986-85-4, LEVAQUIN 102625-70-7, Pantoprazole 105102-22-5, Mometasone 105462-24-6 106266-06-2, RISPERDAL 111025-46-8, Pioglitazone 111974-69-7, Quetiapine 111974-72-2, SEROQUEL 112529-15-4, Actos 113427-24-0, ERYPO 113665-84-2, Clopidogrel 114798-26-4, Losartan 115436-72-1, Actonel 117976-89-3, Rabeprazole 117976-90-6, Aciphex 119141-88-7, Esomeprazole 120202-66-6, PLAVIX 122320-73-4, Rosiglitazone 123143-86-2 124750-99-8, COZAAR 124832-26-4, Valacyclovir 124832-27-5, VALTREX 129318-43-0, FOSAMAX 130209-82-4, XALATAN **131918-61-1**, ZEMPLAR 132539-06-1, ZYPREXA 133107-64-9, HUMALOG 134523-00-5, Atorvastatin 134523-03-8, LIPITOR 137862-53-4, DIOVAN 138402-11-6, AVAPRO 138786-67-1, PROTONIX 151767-02-1, SINGULAIR 153439-40-8, Allegra 155141-29-0, AVANDIA 158966-92-8, Montelukast 161973-10-0, NEXIUM 162011-90-7, VIOXX 169590-42-5, CELEBREX 171599-83-0, VIAGRA 181695-72-7, BEXTRA 330935-97-2 847780-86-3 847780-87-4
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and kits for monitoring resistance to therapeutic agents)

L9 ANSWER 3 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB The invention provides methods of reducing the severity of a proliferative disorder. One method involves administering to an individual having the proliferative disorder an effective amount of paricalcitol, wherein the paricalcitol reduces cellular proliferation, with the proviso that the **cancer** is not prostate **cancer** or head and neck squamous cell **carcinoma**. Another method of reducing the severity of a proliferative disorder provided by the invention involves administering to an individual having the proliferative disorder an effective amount of paricalcitol and an anti-**cancer** agent, wherein the combination of paricalcitol and the anti-**cancer** agent reduces cell proliferation, with the proviso that the proliferative disorder is not prostate **cancer** or head and neck squamous cell **carcinoma**

2004:606361 Document Number 141:134693 Paricalcitol as a chemotherapeutic agent for treating proliferative disorders. Koeffler, Phillip H.; Kumagai, Takashi (Cedars-Sinai Medical Center, USA). PCT Int. Appl. WO 200406

A2 20040729, 99 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US754 20040113. PRIORITY: US 2003-2003/PV439932 20030113.

AB . . . having the proliferative disorder an effective amount of paricalcitol, wherein the paricalcitol reduces cellular proliferation, with the proviso that the **cancer** is not prostate **cancer** or head and neck squamous cell **carcinoma**. Another method of reducing the severity of a proliferative disorder provided by the invention involves administering to an individual having the proliferative disorder an effective amount of paricalcitol and an anti-**cancer** agent, wherein the combination of paricalcitol and the anti-**cancer** agent reduces cell proliferation, with the proviso that the proliferative disorder is not prostate **cancer** or head and neck squamous cell **carcinoma**.

IT **Leukemia**
(acute lymphocytic; paricalcitol, alone or in combination with other drugs, as a chemotherapeutic agent for treating proliferative disorders)

IT **Leukemia**
(acute myeloid; paricalcitol, alone or in combination with other drugs, as a chemotherapeutic agent for treating proliferative disorders)

IT Intestine, **neoplasm**
(colon; paricalcitol, alone or in combination with other drugs, as a chemotherapeutic agent for treating proliferative disorders)

IT Uterus, **neoplasm**
(endometrium; paricalcitol, alone or in combination with other drugs, as a chemotherapeutic agent for treating proliferative disorders)

IT Antitumor agents
Apoptosis
Brain, **neoplasm**
Combination chemotherapy
Human
Leukemia
Lymphoma
Mammary gland, **neoplasm**
Multiple **myeloma**
Myelodysplastic syndromes
Neoplasm
Prostate gland, **neoplasm**
(paricalcitol, alone or in combination with other drugs, as a chemotherapeutic agent for treating proliferative disorders)

IT 50-02-2, Dexamethasone 51-21-8, 5-FU 57-22-7, Vincristine 59-05-2, Methotrexate 1327-53-3, Arsenic trioxide 25316-40-9, Adriamycin 33069-62-4, Taxol 123653-11-2, NS 398 **131918-61-1**, Paricalcitol 179324-69-7, PS-341
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(paricalcitol, alone or in combination with other drugs, as a chemotherapeutic agent for treating proliferative disorders)

L9 ANSWER 4 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB 19-Nor-1α,25-dihydroxyvitamin D2 (paricalcitol) is an analog of

1,25(OH)2D3 with reduced calcemic effects that is approved in the United States for the suppression of parathyroid hormone in chronic renal failure. Paricalcitol has anticancer activity in prostate **cancer** cells. We tested the effects of paricalcitol on the HL-60 **leukemia** cells, studying cellular differentiation, cell cycle changes, apoptosis and cellular proliferation. Paricalcitol at 10-8 M concentration induced the maturation of HL-60 cells in a time-dependent manner, as shown by increased expression of CD11b differentiation surface antigen. The ability of HL-60 cells to reduce nitroblue tetrazolium (NBT) was markedly increased after exposure to paricalcitol at 10-8 M for 72 h. Paricalcitol inhibited colony formation of HL-60 cells in a soft agar semisolid media after 10-day incubation (estimated IC50 of 5+10-9 M). Exposure to 10-8 M paricalcitol for 72 h increased the number of cells in G0/G1 phase, and decreased the number of cells in S phase, and significantly increased the number of HL-60 cells undergoing apoptosis. The concentration required to achieve inhibition of growth of HL-60 cells is comparable to clin. achievable levels. These findings support the clin. evaluation of paricalcitol as an antileukemia agent.

2004:522256 Document Number 141:134637 19-Nor-1α,25-dihydroxyvitamin D2 (paricalcitol) exerts anticancer activity against HL-60 cells in vitro at clinically achievable concentrations. Molnar, Istvan; Kute, Timothy; Willingham, Mark C.; Schwartz, Gary G. (Section on Hematology and Oncology, Department of Internal Medicine, Wake Forest University School of Medicine, Winston-Salem, NC, 27157, USA). Journal of Steroid Biochemistry and Molecular Biology, 89-90(1-5), 539-543 (English) 2004. CODEN: JSBBEZ. ISSN: 0960-0760. Publisher: : Elsevier Science Ltd..

AB . . . in the United States for the suppression of parathyroid hormone in chronic renal failure. Paricalcitol has anticancer activity in prostate **cancer** cells. We tested the effects of paricalcitol on the HL-60 **leukemia** cells, studying cellular differentiation, cell cycle changes, apoptosis and cellular proliferation. Paricalcitol at 10-8 M concentration induced the maturation of. . .

IT Antitumor agents
Apoptosis
Cell cycle
Cell differentiation
Human
Leukemia
(19-Nor-1α,25-dihydroxyvitamin D2 (paricalcitol) exerts anticancer activity against HL-60 cells in vitro at clin. achievable concns.)

IT **131918-61-1**, Paricalcitol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(19-Nor-1α,25-dihydroxyvitamin D2 (paricalcitol) exerts anticancer activity against HL-60 cells in vitro at clin. achievable concns.)

L9 ANSWER 5 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB This invention relates to multi-use dispensing vessels containing pharmaceutical formulations of active vitamin D compds., and also to plastic fill containers containing active vitamin D formulations. The vitamin D formulation comprises an active vitamin D compound or analog; a non-ionic solubilizer; a lipophilic antioxidant, and optionally, an agent(s) that is an organic solvent, a preservative or both, in an aqueous vehicle. The formulation comprises a vitamin D compound or analog, a non-ionic solubilizer, a small amount of lipophilic antioxidant, and optionally, an

agent that includes an organic solvent (e.g., ethanol) or co-solvents (e.g., propylene glycol and ethanol) and/or a preservative (e.g., benzyl alc.). The formulations may be formulated in a variety of concns. in various vial sizes for various administration dosages.

2004:220032 Document Number 140:259103 Multi-use vessels and plastic blow fill containers for active vitamin D formulations. Mazess, Richard B.; Driscoll, Jeffrey W.; Goldensoph, Creighton Reed; Levan, Leon W. (Bone Care International, Inc., USA). U.S. Pat. Appl. Publ. US 2004053895 A1 20040318, 7 pp. (English). CODEN: USXXCO. APPLICATION: US 2002-247766 20020918.

IT Intestine, **neoplasm**
(colon; multi-use vessels and plastic containers for active vitamin D formulations)

IT Antitumor agents
Containers
Hyperparathyroidism
Mammary gland, **neoplasm**
Neoplasm
Pancreas, **neoplasm**
Prostate gland, **neoplasm**
Psoriasis
(multi-use vessels and plastic containers for active vitamin D formulations)

IT Disease, animal
(proliferative, **hyperproliferative**; multi-use vessels and plastic containers for active vitamin D formulations)

IT 64-17-5, Ethanol, biological studies 100-51-6, Benzyl alcohol, biological studies 127-40-2, Lutein 128-37-0, Butylated hydroxytoluene, biological studies 144-68-3, Zeaxanthin 502-65-8, Lycopene 1406-16-2, Vitamin D 1406-18-4, Vitamin E 1406-18-4D, Vitamin E, esters 9004-54-0, Dextrans, biological studies 9005-64-5, TWEEN-20 12441-09-7D, Sorbitan, monoester, polyethylene glycol derivs. 12619-70-4, Cyclodextrins 19891-75-9, Lycophyll 25322-68-3 32222-06-3, Calcitriol 54573-75-0, Doxercalciferol 57828-26-9, Lipoic acid 83805-11-2, Falecalcitriol 103909-75-7, Maxacalcitol 112965-21-6, Calcipotriol **131918-61-1**, Paricalcitol 134404-52-7, Seocalcitol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(multi-use vessels and plastic containers for active vitamin D formulations)

L9 ANSWER 6 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB The invention relates to pharmaceutical formulations of lipophilic therapeutic agents in which such agents are solubilized in largely aqueous vehicles, and processes for preparing and using the same. A formulation was prepared from a vitamin D compound, 1αa-(OH)D2, benzyl alc. 2.5, and Tween-20 0.5-2.5% and BHT 20 ppm. The results of the phase one study indicate that patients treated with the MTD of 1α-(OH)D2 for at least six months report that bone pain associated with metastatic disease is significantly diminished. The results of the phase two study indicate that after 2 yr, CAT scans, x-rays and bone scans used for evaluating the progression of metastatic disease show stable disease or partial remission in many patients treated at the lower dosage, and stable disease and partial or complete remission in many patients treated at the higher dosage. The present invention provides an improved formulation for lipophilic drug agents that are only slightly soluble in an aqueous vehicle.

2004:220031 Document Number 140:259102 Formulation for lipophilic agents.

Mazess, Richard B.; Driscoll, Jeffrey W.; Goldensoph, Creighton Reed; Levan, Leon W. (Bone Care International, Inc., USA). U.S. Pat. Appl. Publ. US 2004053894 A1 20040318, 10 pp. (English). CODEN: USXXCO. APPLICATION: US 2002-247765 20020918.

IT Intestine, **neoplasm**
(colon; formulation for lipophilic antioxidants)

IT Analgesics
Anthelmintics
Anti-inflammatory agents
Antianginal agents
Antiarrhythmics
Antibacterial agents
Anticoagulants
Anticonvulsants
Antidepressants
Antidiabetic agents
Antihypertensives
Antimalarials
Antimigraine agents
Antiobesity agents
Antioxidants
Antiparkinsonian agents
Antipsychotics
Antitumor agents
Antiviral agents
Anxiety
Anxiolytics
Blood coagulation
Cognition enhancers
Diabetes mellitus
Diuresis
Diuretics
Epilepsy
Fungicides
Gastrointestinal agents
Gout
Human
Hyperparathyroidism
Hypertension
Hypnotics and Sedatives
Immunosuppressants
Immunosuppression
Inflammation
Inotropics
Malaria
Mammary gland, **neoplasm**
Muscarinic antagonists
Muscle relaxants
Mycosis
Neoplasm
Obesity
Osteoporosis
Pain
Pancreas, **neoplasm**
Parkinson's disease
Preservatives
Prostate gland, **neoplasm**

Protozoa
Protozoacides
Psoriasis
Sleep
Thyroid gland, disease
(formulation for lipophilic antioxidants)

IT 64-17-5, Ethanol, biological studies 100-51-6, Benzyl alcohol, biological studies 127-40-2, Xanthophyll 128-37-0, Butylated hydroxytoluene, biological studies 144-68-3, Zeaxanthin 502-65-8, Lycopene 1406-16-2, Vitamin D 1406-18-4, Vitamin E 1406-18-4D, Vitamin E, esters 9004-54-0, Dextran, biological studies 9005-64-5, Tween 20 12619-70-4, Cyclodextrin 19891-75-9, Lycophyll 25322-68-3 32222-06-3, Calcitriol 57828-26-9, Lipoic acid 83805-11-2, Falecalcitriol 103909-75-7, Maxacalcitol 112965-21-6, Calcipotriol **131918-61-1**, Paricalcitol 134404-52-7, Seocalcitol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulation for lipophilic antioxidants)

L9 ANSWER 7 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB Prostate **cancer** cells contain specific receptors (VDR) for 1α,25-dihydroxyvitamin D (1α,25(OH)2D), which is known to inhibit the proliferation and invasiveness of these cells. These findings support the use of 1α,25(OH)2D for prostate **cancer** therapy. However, because 1α,25(OH)2D can cause hypercalcemia, analogs of 1α,25(OH)2D that are less calcemic but which exhibit potent antiproliferative activity would be attractive as therapeutic agents. The authors studied 4 vitamin D compds.: 25-hydroxyvitaminD3 [25(OH)D3], which is converted to 1α,25(OH)2D3 in prostate cells, and 3 analogs of 1α,25(OH)2D3: EB1089, 19-nor-1α,25(OH)2D2 and hexafluoro-1α,25(OH)2D3 (F6-1α,25(OH)2D3). 19-Nor-1α,25(OH)2D2 was shown to be less calcemic than 1α,25(OH)2D3 in clin. trials. F6-1α,25(OH)2D3 was shown to be 100-fold more active than 1α,25(OH)2D3 and to be longer-lasting in inhibiting keratinocyte proliferation in vitro. EB1089 was shown to be less calcemic than 1α,25(OH)2D3 in rats implanted with Leydig cell **tumors**. For 25(OH)D3, 19-nor-1α,25(OH)2D2 and F6-1α,25(OH)2D3, the authors studied the in vitro effects and compared their activity to 1α,25(OH)2D3 on cellular proliferation by 3H-thymidine incorporation assay. In addition, the authors studied transactivation of the VDR in the presence of 25(OH)D3 and 19-nor-1α,25(OH)2D2 in prostate cells. For EB1089, we compared its inhibition of prostate **cancer** metastasis to that induced by 1α,25(OH)2D3 in vivo in the rat Dunning MAT LyLu prostate **cancer** model. The authors found that 1α,25(OH)2D3 and 19-nor-1α,25(OH)2D2 caused similar dose-dependent inhibition in 3H-thymidine incorporation into DNA in prostate cells and behaved similarly in the CAT reporter gene transactivation assay in PC-3/VDR cells. F6-1α,25(OH)2D3 is 10- to 50-fold more active than 1α,25(OH)2D3 in 3H-thymidine incorporation into DNA in the primary cultured prostate cells. Likewise, 25(OH)D3 had comparable antiproliferative activity to 1α,25(OH)2D3. In the rat model, **tumor** vols. and the number of metastases in the lungs were significantly reduced by both 1α,25(OH)2D3 (10.4 ± 2.81 **tumor** foci) and EB1089 (7.7±1.29 **tumor** foci) compared to controls (22.7 ± 1.98 **tumor** foci). Although serum calcium levels were significantly elevated in both 1α,25(OH)2D3- and EB1089-treated rats, EB1089 was significantly less calcemic than

1α,25(OH)2D3 (12.59±0.21 mg/dL vs. 14.47±.46 mg/dL; 1 μg/kg; p<0.001). In conclusion, the authors' data indicate that 25(OH)D3 and the 3 1α,25(OH)2D analogs represent 2 different solns. to the problem of hypercalcemia associated with vitamin D-based prostate **cancer** therapies: 25(OH)D3 requires the presence of 25-hydroxyvitaminD-1α-hydroxylase, whereas 19-nor-1α,25(OH)2D2, F6-1α,25(OH)2D3 and EB1089 do not. These compds. may be good candidates for human clin. trials in prostate **cancer**.

2003:748383 Document Number 140:71446 Evaluation of vitamin D analogs as therapeutic agents for prostate **cancer**. Chen, Tai C.; Holick, Michael F.; Lokeshwar, Bal L.; Burnstein, Kerry L.; Schwartz, Gary G. (Department of Medicine, Endocrine Section, Boston University School of Medicine, Boston, MA, 02118, USA). Recent Results in Cancer Research, 164(Vitamin D Analogs in Cancer Prevention and Therapy), 273-288 (English) 2003. CODEN: RRCRBU. ISSN: 0080-0015. Publisher: Springer-Verlag.

TI Evaluation of vitamin D analogs as therapeutic agents for prostate **cancer**

AB Prostate **cancer** cells contain specific receptors (VDR) for 1α,25-dihydroxyvitamin D (1α,25(OH)2D), which is known to inhibit the proliferation and invasiveness of these cells. These findings support the use of 1α,25(OH)2D for prostate **cancer** therapy. However, because 1α,25(OH)2D can cause hypercalcemia, analogs of 1α,25(OH)2D that are less calcemic but which exhibit potent antiproliferative activity. . . inhibiting keratinocyte proliferation in vitro. EB1089 was shown to be less calcemic than 1α,25(OH)2D3 in rats implanted with Leydig cell **tumors**. For 25(OH)D3, 19-nor-1α,25(OH)2D2 and F6-1α,25(OH)2D3, the authors studied the in vitro effects and compared their activity to 1α,25(OH)2D3 on cellular. . . the VDR in the presence of 25(OH)D3 and 19-nor-1α,25(OH)2D2 in prostate cells. For EB1089, we compared its inhibition of prostate **cancer** metastasis to that induced by 1α,25(OH)2D3 in vivo in the rat Dunning MAT LyLu prostate **cancer** model. The authors found that 1α,25(OH)2D3 and 19-nor-1α,25(OH)2D2 caused similar dose-dependent inhibition in 3H-thymidine incorporation into DNA in prostate cells. . . into DNA in the primary cultured prostate cells. Likewise, 25(OH)D3 had comparable antiproliferative activity to 1α,25(OH)2D3. In the rat model, **tumor** vols. and the number of metastases in the lungs were significantly reduced by both 1α,25(OH)2D3 (10.4 ± 2.81 **tumor** foci) and EB1089 (7.7±1.29 **tumor** foci) compared to controls (22.7 ± 1.98 **tumor** foci). Although serum calcium levels were significantly elevated in both 1α,25(OH)2D3- and EB1089-treated rats, EB1089 was significantly less calcemic than. . . 25(OH)D3 and the 3 1α,25(OH)2D analogs represent 2 different solns. to the problem of hypercalcemia associated with vitamin D-based prostate **cancer** therapies: 25(OH)D3 requires the presence of 25-hydroxyvitaminD-1α-hydroxylase, whereas 19-nor-1α,25(OH)2D2, F6-1α,25(OH)2D3 and EB1089 do not. These compds. may be good candidates for human clin. trials in prostate **cancer**.

ST vitamin D analog receptor antitumor prostate **cancer**; dihydroxyvitamin D3 Seocalcitol antitumor vitamin D receptor prostate gland

IT Prostate gland, **neoplasm**
(metastasis; vitamin D analogs as therapeutic agents for prostate **cancer**)

IT Antitumor agents
Cell proliferation
Human
Prostate gland, **neoplasm**
(vitamin D analogs as therapeutic agents for prostate **cancer**)
IT Vitamin D receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(vitamin D analogs as therapeutic agents for prostate **cancer**)
IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood serum; vitamin D analogs as therapeutic agents for prostate **cancer**)
IT 19356-17-3, 25-HydroxyvitaminD3 32222-06-3, 1α,25-Dihydroxyvitamin D3 83805-11-2 **131918-61-1** 134404-52-7, Seocalcitol
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vitamin D analogs as therapeutic agents for prostate **cancer**)

L9 ANSWER 8 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN
AB Radiotherapy with external beam radiation or brachytherapy is an established therapeutic modality for prostate **cancer**. Approx. 30% of patients with localised prostate **cancer** relapse at the irradiated site. Secondary effects of ionising radiation (IR), for example, bowel and bladder complications, are common. Thus, the search for biol. response modifiers that could potentiate the therapeutic effects of radiation and limit the occurrence of serious side effects is an important task in prostate **cancer** therapy. 1α,25-Dihydroxyvitamin D3 (calcitriol), the active metabolite of vitamin D, and its analogs are under investigation for the treatment of several malignancies including prostate **cancer**. Here, we report that 1α,25-dihydroxyvitamin D3 and its less calcemic analog 19-nor-1α,25-(OH)2D2 (Zemplar) act synergistically with IR to inhibit the growth of the human prostate **cancer** cells in vitro. 1α,25-Dihydroxyvitamin D3 potentiated IR-induced apoptosis of LNCaP cells, and nanomolar doses of 1α,25-dihydroxyvitamin D3 and 19-nor-1α,25-(OH)2D2 showed synergistic inhibition of growth of LNCaP cells at radiobiol. relevant doses of IR (1-2Gy). At higher doses of IR, the combination of 1α,25-dihydroxyvitamin D3 and IR or 19-nor-1α,25-(OH)2D2 and IR resulted in moderate antagonism. The synergistic effect at radiobiol. relevant doses of radiation suggests that a combination of 1α,25-dihydroxyvitamin D3 or 19-nor-1α,25-(OH)2D2 with IR could permit a reduction in the dose of radiation given clin. and thus potentially reduce treatment-related morbidity.
2003:616938 Document Number 140:334734 1α,25-Dihydroxyvitamin D3 (calcitriol) and its analogue, 19-nor-1α,25(OH)2D2, potentiate the effects of ionising radiation on human prostate **cancer** cells.
Dunlap, N.; Schwartz, G. G.; Eads, D.; Cramer, S. D.; Sherk, A. B.; John, V.; Koumenis, C. (Department of Radiation Oncology, Comprehensive Cancer Center of Wake Forest University School of Medicine, Winston-Salem, NC, 27157, USA). British Journal of Cancer, 89(4), 746-753 (English) 2003. CODEN: BJCAAI. ISSN: 0007-0920. Publisher: Nature Publishing Group.
TI 1α,25-Dihydroxyvitamin D3 (calcitriol) and its analogue, 19-nor-1α,25(OH)2D2, potentiate the effects of ionising radiation on human prostate **cancer** cells
AB Radiotherapy with external beam radiation or brachytherapy is an established therapeutic modality for prostate **cancer**. Approx. 30% of patients with localised prostate **cancer** relapse at the

irradiated site. Secondary effects of ionising radiation (IR), for example, bowel and bladder complications, are common. Thus,. . . potentiate the therapeutic effects of radiation and limit the occurrence of serious side effects is an important task in prostate **cancer** therapy. 1α,25-Dihydroxyvitamin D3 (calcitriol), the active metabolite of vitamin D, and its analogs are under investigation for the treatment of several malignancies including prostate **cancer**. Here, we report that 1α,25-dihydroxyvitamin D3 and its less calcemic analog 19-nor-1α,25-(OH)2D2 (Zemplar) act synergistically with IR to inhibit the growth of the human prostate **cancer** cells in vitro. 1α,25-Dihydroxyvitamin D3 potentiated IR-induced apoptosis of LNCaP cells, and nanomolar doses of 1α,25-dihydroxyvitamin D3 and 19-nor-1α,25-(OH)2D2 showed. . .

ST prostate **cancer** radiotherapy calcitriol Zemplar synergy

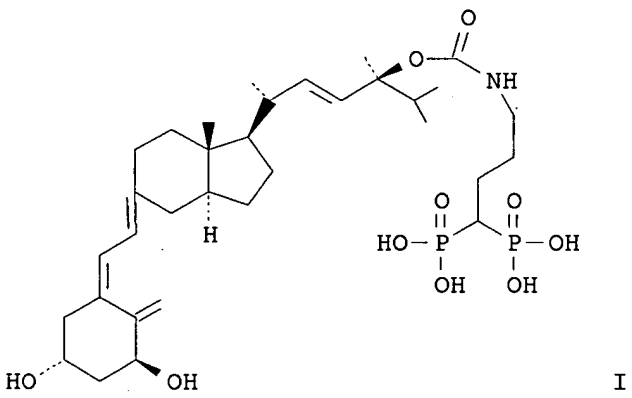
IT Antitumor agents
Human
Prostate gland, **neoplasm**
(calcitriol and Zemplar potentiate effects of ionising radiation on human prostate **cancer**)

IT Drug interactions
(synergistic; calcitriol and Zemplar potentiate effects of ionising radiation on human prostate **cancer**)

IT 32222-06-3, 1α,25-Dihydroxyvitamin D3 **131918-61-1**, Zemplar
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(calcitriol and Zemplar potentiate effects of ionising radiation on human prostate **cancer**)

L9 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

GI



I

AB The present invention is directed to a conjugate which includes at least one vitamin D moiety and at least one targeting mol. moiety to pharmaceutical compns. of the conjugate, and to methods for using the conjugate for target-specific delivery of vitamin D or analogs to tissues. When a particularly preferred form is administered to a patient, the targeting mol. component of the conjugate of this invention seeks out and binds to a tissue of interest, such as bone or **tumor** tissue, where the vitamin D has a therapeutic effect. One example compound prepared

was I.

2003:532131 Document Number 139:101329 Targeted therapeutic delivery of vitamin D compounds. Mazess, Richard B.; Bishop, Charles W. (Bone Care International, Inc., USA). U.S. Pat. Appl. Publ. US 2003129194 A1 20030710, 28 pp., Cont.-in-part of U.S. Ser. Number 402,636. (English). CODEN: USXXCO. APPLICATION: US 2002-251905 20020920. PRIORITY: US 1997-PV38364 19970213; WO 1998-US2899 19980213; US 2000-402636 20000426.

AB . . . component of the conjugate of this invention seeks out and binds to a tissue of interest, such as bone or **tumor** tissue, where the vitamin D has a therapeutic effect. One example compound prepared was I.

IT 1406-16-2D, Vitamin d, conjugates 2809-21-4 10596-23-3 32222-06-3, 1α,25-Dihydroxyvitamin D3 40391-99-9 41294-56-8, 1α-Hydroxyvitamin D3 54573-75-0, 1α-Hydroxyvitamin D2 60133-18-8, 1α,25-Dihydroxyvitamin D2 66376-36-1, Alendronate 83805-11-2, Falecalcitriol 89987-06-4, Tiludronate 103909-75-7, Maxacalcitol 105462-24-6 112965-21-6, Calcipotriol 114084-78-5, Ibandronate 118072-93-8, Zoledronate 124043-51-2, 1α,24-Dihydroxyvitamin D2 131249-38-2, 1α,25-Dihydroxyvitamin D4 **131918-61-1**, Paricalcitol 134404-52-7, Seocalcitol 157893-62-4, 1α,24-Dihydroxyvitamin D4
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeted therapeutic delivery of vitamin D compds.)

L9 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB 1,25-Dihydroxyvitamin D3 inhibits growth of several types of human **cancer** cells in vitro, but its therapeutic use is hampered because it causes hypercalcemia. 19-Nor-1,25-Dihydroxyvitamin D2 (paricalcitol) is a noncalcemic vitamin D analog that is approved by the Food and Drug Administration for the treatment of secondary hyperparathyroidism. The authors investigated the antitumor activity and mechanism of action of paricalcitol in vitro and in vivo. Effects of paricalcitol on proliferation, the cell cycle, differentiation, and apoptosis were examined in **cancer** cell lines. Effects on **tumor** growth were examined with colon **cancer** cell xenografts in nude mice (five in the exptl. group and five in the control group). The interaction of paricalcitol with the vitamin D receptor (VDR) in mononuclear spleen cells and myeloid stem cells from wild-type and VDR knockout mice was examined All statistical tests were two-sided. Paricalcitol inhibited the proliferation of myeloid **leukemia** cell lines HL-60, NB-4, and THP-1 cells at an ED that inhibited growth 50% (ED50) of 2.4-5.8 + 10-9 M by inducing cell cycle arrest and differentiation. Paricalcitol inhibited the proliferation of NCI-H929 **myeloma** cells at an ED50 of 2.0 + 10-10 M by inducing cell cycle arrest and apoptosis. Paricalcitol also inhibited the proliferation of colon **cancer** cell lines HT-29 (ED50 = 1.7 + 10-8 M) and SW837 (ED50 = 3.2 + 10-8 M). HT-29 colon **cancer** xenografts in paricalcitol-treated nude mice were smaller (1044 Mm3 and 1752 Mm3, difference = 708 Mm3, 95% confidence interval = 311 to 1104 Mm3) and weighed less (1487 mg and 4162 mg, difference = 2675 mg, 95% confidence interval = 2103 to 3248 mg) than those in vehicle-treated mice. Paricalcitol induced committed myeloid hematopoietic stem cells from wild-type but not from VDR knockout mice to differentiate as macrophages. Thus, paricalcitol has anticancer activity against myeloid **leukemia**, **myeloma**, and colon **cancer** cells that may be mediated through the VDR. Because it has been approved by the Food and Drug Administration, clin. trials of this agent in certain **cancers** are reasonable.

2003:480563 Document Number 139:317916 Vitamin D2 Analog 19-nor-1,25-

Dihydroxyvitamin D2: Antitumor Activity Against **Leukemia, Myeloma,** and Colon **Cancer** Cells. Kumagai, Takashi; O'Kelly, James; Said, Jonathan W.; Koeffler, H. Phillip (Div. Hematol./Oncol., Dep. Med., University California at Los Angeles Sch. Med., Los Angeles, CA, 90048, USA). Journal of the National Cancer Institute, 95(12), 896-905 (English) 2003. CODEN: JNCIEQ. ISSN: 0027-8874. Publisher: Oxford University Press.

TI Vitamin D2 Analog 19-nor-1,25-Dihydroxyvitamin D2: Antitumor Activity Against **Leukemia, Myeloma,** and Colon **Cancer** Cells

AB 1,25-Dihydroxyvitamin D3 inhibits growth of several types of human **cancer** cells in vitro, but its therapeutic use is hampered because it causes hypercalcemia. 19-Nor-1,25-Dihydroxyvitamin D2 (paricalcitol) is a noncalcemic vitamin. . . paricalcitol in vitro and in vivo. Effects of paricalcitol on proliferation, the cell cycle, differentiation, and apoptosis were examined in **cancer** cell lines. Effects on **tumor** growth were examined with colon **cancer** cell xenografts in nude mice (five in the exptl. group and five in the control group). The interaction of paricalcitol. . . cells from wild-type and VDR knockout mice was examined All statistical tests were two-sided. Paricalcitol inhibited the proliferation of myeloid **leukemia** cell lines HL-60, NB-4, and THP-1 cells at an ED that inhibited growth 50% (ED50) of 2.4-5.8 + 10-9 M by inducing cell cycle arrest and differentiation. Paricalcitol inhibited the proliferation of NCI-H929 **myeloma** cells at an ED50 of 2.0 + 10-10 M by inducing cell cycle arrest and apoptosis. Paricalcitol also inhibited the proliferation of colon **cancer** cell lines HT-29 (ED50 = 1.7 + 10-8 M) and SW837 (ED50 = 3.2 + 10-8 M). HT-29 colon **cancer** xenografts in paricalcitol-treated nude mice were smaller (1044 Mm3 and 1752 Mm3, difference = 708 Mm3, 95% confidence interval =. . . cells from wild-type but not from VDR knockout mice to differentiate as macrophages. Thus, paricalcitol has anticancer activity against myeloid **leukemia, myeloma,** and colon **cancer** cells that may be mediated through the VDR. Because it has been approved by the Food and Drug Administration, clin. trials of this agent in certain **cancers** are reasonable.

ST vitamin D2 analog paricalcitol antitumor **leukemia myeloma** colon **cancer;** nordihydroxyvitamin D3 antitumor **leukemia myeloma** colon **cancer**

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bcl-2; vitamin D2 analog paricalcitol antitumor activity against **leukemia, myeloma,** and colon **cancer** cells and mechanisms thereof)

IT Cyclins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D1; vitamin D2 analog paricalcitol antitumor activity against **leukemia, myeloma,** and colon **cancer** cells and mechanisms thereof)

IT Antitumor agents
Intestine, **neoplasm**
(colon; vitamin D2 analog paricalcitol antitumor activity against **leukemia, myeloma,** and colon **cancer** cells and mechanisms thereof)

IT Cell proliferation
(inhibition; vitamin D2 analog paricalcitol antitumor activity against **leukemia, myeloma,** and colon **cancer** cells

and mechanisms thereof)
IT Antitumor agents
(**leukemia**; vitamin D2 analog paricalcitol antitumor activity against **leukemia**, **myeloma**, and colon **cancer** cells and mechanisms thereof)
IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(myc; vitamin D2 analog paricalcitol antitumor activity against **leukemia**, **myeloma**, and colon **cancer** cells and mechanisms thereof)
IT **Leukemia**
(myelogenous; vitamin D2 analog paricalcitol antitumor activity against **leukemia**, **myeloma**, and colon **cancer** cells and mechanisms thereof)
IT Hematopoietic precursor cell
(myeloid; vitamin D2 analog paricalcitol antitumor activity against **leukemia**, **myeloma**, and colon **cancer** cells and mechanisms thereof)
IT Antitumor agents
(**myeloma**; vitamin D2 analog paricalcitol antitumor activity against **leukemia**, **myeloma**, and colon **cancer** cells and mechanisms thereof)
IT Cyclin dependent kinase inhibitors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(p21CIP1; vitamin D2 analog paricalcitol antitumor activity against **leukemia**, **myeloma**, and colon **cancer** cells and mechanisms thereof)
IT Cyclin dependent kinase inhibitors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(p27KIP1; vitamin D2 analog paricalcitol antitumor activity against **leukemia**, **myeloma**, and colon **cancer** cells and mechanisms thereof)
IT Spleen
(splenocyte; vitamin D2 analog paricalcitol antitumor activity against **leukemia**, **myeloma**, and colon **cancer** cells and mechanisms thereof)
IT Apoptosis
Cell cycle
Cell differentiation
Human
Macrophage
Multiple **myeloma**
(vitamin D2 analog paricalcitol antitumor activity against **leukemia**, **myeloma**, and colon **cancer** cells and mechanisms thereof)
IT Vitamin D receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(vitamin D2 analog paricalcitol antitumor activity against **leukemia**, **myeloma**, and colon **cancer** cells and mechanisms thereof)
IT 7440-70-2, Calcium, biological studies 53112-53-1, 25-Hydroxyvitamin D3-24-hydroxylase 301166-54-1 329900-75-6, COX-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(vitamin D2 analog paricalcitol antitumor activity against **leukemia**, **myeloma**, and colon **cancer** cells and mechanisms thereof)
IT **131918-61-1**, 19-Nor-1,25-Dihydroxyvitamin D2

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vitamin D2 analog paricalcitol antitumor activity against **leukemia**, **myeloma**, and colon **cancer** cells and mechanisms thereof)

L9 ANSWER 11 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN
AB The invention relates to therapeutics for the prevention and treatment of vitamin D responsive diseases in humans, as well as other animals, through the use of biol. active vitamin D compds. in combination with at least one other immunomodulatory compound such as interleukin-10, interleukin-4, or a TNF-α inhibitor.
2003:455025 Document Number 139:30856 Treating vitamin D responsive diseases. Hayes, Colleen E.; Nashold, Faye E. (Northern Lights Pharmaceuticals, LLC, USA). U.S. Pat. Appl. Publ. US 2003109506 A1 20030612, 27 pp., Cont.-in-part of U.S. Ser. Number 469,985. (English). CODEN: USXXCO. APPLICATION: US 2002-170746 20020613. PRIORITY: US 1999-469985 19991221; WO 2000-US34913 20001221.
IT Hemoglobins
Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(treating vitamin D responsive diseases)
IT 103656-37-7 131875-08-6, KH1060 **131918-61-1** 195051-26-4
215714-87-7 233268-76-3, LG 190090 233268-77-4, LG190119
233268-78-5, LG190155 233268-79-6, LG 190176 233268-81-0, LG 190178
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treating vitamin D responsive diseases)

L9 ANSWER 12 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN
AB Purpose: 19-Nor-1α,25-dihydroxyvitamin D2 (paricalcitol) is an analog of 1,25(OH)2D3 with reduced calcemic effects that is approved for the suppression of parathyroid hormone in chronic renal failure. Paricalcitol has recently been reported to have anticancer activity in prostate **cancer**. In order to explore paricalcitol as a potential agent against **leukemia**, we tested its effects on HL-60 and U937 **leukemia** cell lines. Methods: We studied cellular differentiation via expression of CD11b and CD14 surface antigens using flow cytometry, and via the nitroblue tetrazolium (NBT) assay. Cell cycle was analyzed using propidium iodide staining. Apoptosis was assessed with the annexin V assay. Cellular proliferation was determined via colony inhibition on semisolid medium. Results: Paricalcitol induced the maturation of HL-60 and U937 cells, as shown by increased expression of CD11b differentiation surface antigen. CD14 showed increased expression in HL-60 but not in U937 cells. After exposure to paricalcitol at 10-8 M for 72 h, the ability of HL-60 cells to reduce NBT was markedly increased. Conversely, U937 cells were unchanged. Paricalcitol inhibited colony formation of both HL-60 and U937 cell lines in semisolid medium after a 10-day incubation (estimated IC50 of 3 + 10-8 M in HL-60 cells and 4 + 10-8 M in U937 cells). Paricalcitol at 10-8 M and 10-7 M caused a significant dose- and time-dependent increase of apoptosis in HL60 cells. In both HL-60 and U937 cells, exposure to 10-7 M paricalcitol for 72 h increased the number of cells in G0/G1 phase, and decreased the number of cells in S phase. Conclusions: Paricalcitol inhibits colony formation, induces maturation and causes cell cycle arrest in HL-60 and U937 cells. Addnl., paricalcitol induces apoptosis in HL-60 cells. These findings support the further evaluation of paricalcitol as an antileukemia agent.
2003:379404 Document Number 139:316824 19-Nor-1α,25-dihydroxyvitamin D2

(paricalcitol): effects on clonal proliferation, differentiation, and apoptosis in human **leukemic** cell lines. Molnar, Istvan; Kute, Timothy; Willingham, Mark C.; Powell, Bayard L.; Dodge, William H.; Schwartz, Gary G. (Department of Internal Medicine, Section on Hematology and Oncology, Wake Forest University School of Medicine, Winston-Salem, NC, 27157, USA). Journal of Cancer Research and Clinical Oncology, 129(1), 35-42 (English) 2003. CODEN: JCROD7. ISSN: 0171-5216. Publisher: Springer-Verlag.

TI 19-Nor-1α,25-dihydroxyvitamin D2 (paricalcitol): effects on clonal proliferation, differentiation, and apoptosis in human **leukemic** cell lines

AB . . . the suppression of parathyroid hormone in chronic renal failure. Paricalcitol has recently been reported to have anticancer activity in prostate **cancer**. In order to explore paricalcitol as a potential agent against **leukemia**, we tested its effects on HL-60 and U937 **leukemia** cell lines. Methods: We studied cellular differentiation via expression of CD11b and CD14 surface antigens using flow cytometry, and via. . .

ST nordihydroxyvitamin D2 **leukemia** differentiation apoptosis antitumor; paricalcitol **leukemia** differentiation apoptosis antitumor

IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD11B; paricalcitol effects on clonal proliferation and differentiation and apoptosis in human **leukemic** cell lines)

IT Interphase (cell cycle)
(G0-phase; paricalcitol effects on clonal proliferation and differentiation and apoptosis in human **leukemic** cell lines)

IT Interphase (cell cycle)
(G1-phase; paricalcitol effects on clonal proliferation and differentiation and apoptosis in human **leukemic** cell lines)

IT Interphase (cell cycle)
(S-phase; paricalcitol effects on clonal proliferation and differentiation and apoptosis in human **leukemic** cell lines)

IT Cell proliferation
(inhibition; paricalcitol effects on clonal proliferation and differentiation and apoptosis in human **leukemic** cell lines)

IT Antitumor agents
Apoptosis
Cell cycle
Cell differentiation
Human
Leukemia
(paricalcitol effects on clonal proliferation and differentiation and apoptosis in human **leukemic** cell lines)

IT CD14 (antigen)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(paricalcitol effects on clonal proliferation and differentiation and apoptosis in human **leukemic** cell lines)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αM; paricalcitol effects on clonal proliferation and differentiation and apoptosis in human **leukemic** cell lines)

IT **131918-61-1**, Paricalcitol
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(paricalcitol effects on clonal proliferation and differentiation and

apoptosis in human **leukemic** cell lines)

L9 ANSWER 13 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN
AB Synthetic ligands for the vitamin D receptor (VDR) are potential therapeutic agents for metabolic, **neoplastic**, and autoimmune disorders. Some of these ligands have similar or more potent antiproliferative, yet reduced hypercalcemic actions, than calcitriol. However, the mechanisms for these differential actions have not been clearly defined. We hypothesized that these gene- and tissue-specific effects may relate to ligand-directed selective recruitment of transcriptional coactivators. To identify key elements in ligand structure that facilitate VDR-coactivator interactions, the current studies assessed the ability of the VDR to recruit the coactivators GRIP1 and RAC3 following activation by a series of 20-R- and 20-S (20-epi)-modified analogs. The strength of VDR-coactivator interactions was ligand-specific and did not always correlate with ligand-receptor binding affinity. In general, the 20-epi analogs enhanced these interactions, whereas the 20-R-modified analogs were less effective than calcitriol. The 16-ene,23-yne modification and fluorinated substituents to the side-chain attenuated interaction with coactivators. The enhanced ability of the VDR to recruit GRIP1 following activation by the 20-epi analogs was consistent with potentiation of 20-epi analog-induced transactivation of the osteocalcin gene promoter by GRIP1. Overall, the structure of the ligand side-chain as well as its orientation seemed to affect the avidity of coactivator binding. These results suggest that selective recruitment of coactivators may contribute to gene- and tissue-specific effects of vitamin D analogs.
2002:400748 Document Number 137:332734 Vitamin D analogue-specific recruitment of vitamin D receptor coactivators. Issa, Laura L.; Leong, Gary M.; Sutherland, Robert L.; Eisman, John A. (Bone and Mineral Program, Garvan Institute of Medical Research, Sydney, Australia). Journal of Bone and Mineral Research, 17(5), 879-890 (English) 2002. CODEN: JBMREJ. ISSN: 0884-0431. Publisher: American Society for Bone and Mineral Research.
AB Synthetic ligands for the vitamin D receptor (VDR) are potential therapeutic agents for metabolic, **neoplastic**, and autoimmune disorders. Some of these ligands have similar or more potent antiproliferative, yet reduced hypercalcemic actions, than calcitriol. However,. . .
IT Human
(effects of vitamin D analogs on specific recruitment of vitamin D receptor coactivators in human breast **cancer** T-47D cells)
IT 32222-06-3, Ro21-5535 58702-12-8 103909-75-7, 22-Oxacalcitriol 118694-43-2, Ro23-7553 124409-59-2, Ro24-2287 131875-08-6, KH 1060 **131918-61-1**, 19-Nor-1,25-dihydroxyvitamin D2 134523-84-5, MC 1288 134523-85-6, MC 1301 137102-93-3, Ro24-5531 156208-06-9, Ro25-6760 199798-65-7, Ro 25-8845 216244-44-9, Ro 26-5924
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of vitamin D analogs on specific recruitment of vitamin D receptor coactivators)

L9 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN
AB Methods are disclosed for the regulation of cell differentiation and proliferation, e.g., for treating **hyperproliferative** skin disorder, such as psoriasis, and skin **cancer** for enhancing wound healing, for stimulating hair growth and inhibiting hair growth, by administration of nucleic acid mols. encoding parathyroid hormone (PTH),

parathyroid related peptide (PTHrP), or fragment, analog or derivative thereof, and salts thereof, encapsulated by particular liposomes or incorporated into a porous biocompatible matrix. The nucleic acids can be optionally be administered with an active vitamin D compound Drug formulations containing the nucleic acids of the invention are also claimed.

2002:275817 Document Number 136:273570 Regulation of cell proliferation and differentiation of skin or hair cells using topically applied nucleic acid molecules that encode PTH, PTHrP, their fragments, analogs, or derivatives. Holick, Michael F. (USA). PCT Int. Appl. WO 2002028420 A2 20020411, 56 pp. DESIGNATED STATES: W: AU, CA, JP, KR, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US31082 20011005. PRIORITY: US 2000-2000/PV238134 20001006.

AB Methods are disclosed for the regulation of cell differentiation and proliferation, e.g., for treating **hyperproliferative** skin disorder, such as psoriasis, and skin **cancer** for enhancing wound healing, for stimulating hair growth and inhibiting hair growth, by administration of nucleic acid mols. encoding parathyroid. . .

IT Skin, **neoplasm**
(inhibitors; regulation of cell proliferation and differentiation of skin or hair cells using topically applied nucleic acids encoding PTH, PTHrP, their fragments or analogs optionally in combination with a vitamin D compound)

IT 1406-16-2, Vitamin D 32222-06-3, 1,25-Dihydroxyvitamin D3 112965-21-6, Calcipotriene 130447-37-9 **131918-61-1**
RL: COS (Cosmetic use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(regulation of cell proliferation and differentiation of skin or hair cells using topically applied nucleic acids encoding PTH, PTHrP, their fragments or analogs optionally in combination with a vitamin D compound)

L9 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB Calcitriol has shown a benefit in various small uncontrolled studies of ex vivo immune function. We hypothesized that paricalcitol, a new vitamin D derivative, will have a pos. effect on the immune system with minimal adverse effects on calcium homeostasis. Thirty-one hemodialysis patients not administered vitamin D because of low intact parathyroid hormone (PTH) levels were randomized to placebo or 4 μg of paricalcitol i.v. with the hemodialysis session three times weekly for 12 wk. Effects on in vivo and ex vivo assessments of immune function were evaluated. All patients achieved the target dose of paricalcitol. Twenty patients were anergic at the start of the study; 4 of 11 patients in the paricalcitol group and 0 of 9 patients in the placebo group converted to reactive ($P = 0.09$). The in vivo response to standard hepatitis B booster vaccine and in vitro proliferation and release of interleukin-2 (IL-2), IL-6, **tumor** necrosis factor-α, and interferon-γ from stimulated lymphocytes were not different between the groups. In contrast to clin. immune effects, paricalcitol increased serum calcium levels and decreased PTH and bone alkaline phosphatase levels (all $P < 0.05$). However, hypercalcemia was infrequent. In vitro expts. showed that paricalcitol led to greater dose-dependent thymidine uptake than calcitriol in lymphocytes isolated from either dialysis patients or control subjects. Paricalcitol has a tendency toward improving delayed hypersensitivity reactions, but did not have other proimmune effects. However, as expected, paricalcitol had significant effects on calcium homeostasis compared with placebo. Thus, patients with low PTH levels are unlikely to experience the proimmune effects of vitamin D therapy without more

profound and potentially adverse oversuppression of PTH.

2001:776314 Document Number 136:64597 A placebo-controlled trial to evaluate immunomodulatory effects of paricalcitol. Moe, Sharon M.; Zekonis, Mindaugas; Harezlak, Jaroslaw; Ambrosius, Walter T.; Gassensmith, Christine M.; Murphy, Cynthia L.; Russell, Regina R.; Batiuk, Thomas D. (Department of Medicine, Divisions of Nephrology and Biostatistics, Indiana University School of Medicine, Indianapolis, IN, 46202, USA). American Journal of Kidney Diseases, 38(4), 792-802 (English) 2001. CODEN: AJKDDP. ISSN: 0272-6386. Publisher: W. B. Saunders Co..

AB . . . The in vivo response to standard hepatitis B booster vaccine and in vitro proliferation and release of interleukin-2 (IL-2), IL-6, **tumor** necrosis factor-α, and interferon-γ from stimulated lymphocytes were not different between the groups. In contrast to clin. immune effects, paricalcitol. . .

IT **131918-61-1**, Paricalcitol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunomodulatory effects of paricalcitol, a new vitamin D derivative)

L9 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB The present invention provides solid pharmaceutical compns. for improved delivery of a wide variety of pharmaceutical active ingredients contained therein or sep. administered. In one embodiment, the solid pharmaceutical composition includes a solid carrier, the solid carrier including a substrate and an encapsulation coat on the substrate. The encapsulation coat can include different combinations of pharmaceutical active ingredients, hydrophilic surfactant, lipophilic surfactants and triglycerides. In another embodiment, the solid pharmaceutical composition includes a solid carrier, the solid carrier being formed of different combinations of pharmaceutical active ingredients, hydrophilic surfactants, lipophilic surfactants and triglycerides. The compns. of the present invention can be used for improved delivery of hydrophilic or hydrophobic pharmaceutical active ingredients, such as drugs, nutritionals, cosmeceuticals and diagnostic agents. A composition contained glyburide 1, PEG 40 stearate 33, glycerol monolaurate 17, and nonpareil seed 80 g.

2001:396644 Document Number 135:24671 Solid carriers for improved delivery of active ingredients in pharmaceutical compositions. Patel, Manesh V.; Chen, Feng-jing (Lipocine, Inc., USA). PCT Int. Appl. WO 2001037808 A1 20010531, 107 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US32255 20001122. PRIORITY: US 1999-447690 19991123.

IT Fusion proteins (chimeric proteins)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor** necrosis factor receptor:Fc region; solid carriers for improved delivery of active ingredients in pharmaceutical compns.)

IT 68506-86-5, Vigabatrin 69049-74-7, Nedocromil sodium 69655-05-6, Didanosine 69756-53-2, Halofantrine 70288-86-7, Ivermectin 70458-92-3, Pefloxacin 70458-96-7, Norfloxacin 71486-22-1, Vinorelbine 72432-03-2, Miglitol 72559-06-9, Rifabutine 73384-59-5, Ceftriaxone 73590-58-6, Omeprazole 73963-72-1, Cilostazol 74011-58-8, Enoxacin 74103-06-3, Ketorolac 74356-00-6, Cefotetan disodium 74381-53-6,

Leuprolide acetate 75330-75-5, Lovastatin 75706-12-6, Leflunomide 76420-72-9, Enalaprilat 76470-66-1, Loracarbef 76547-98-3, Lisinopril 76824-35-6, Famotidine 76963-41-2, Nizatidine 78110-38-0, Aztreonam 79350-37-1, Cefixime 79517-01-4, Octreotide acetate 79617-96-2, Sertraline 79794-75-5, Loratadine 79902-63-9, Simvastatin 81093-37-0, Pravastatin 81098-60-4, Cisapride 81103-11-9, Clarithromycin 81161-17-3, Esmolol hydrochloride 82410-32-0, Ganciclovir 82419-36-1, Ofloxacin 82626-48-0, Zolpidem 82952-64-5, Trimetrexate glucuronate 83799-24-0, Fexofenadine 83869-56-1, Granulocyte-macrophage colony stimulating factor 83881-51-0, Cetirizine 83905-01-5, Azithromycin 84057-84-1, Lamotrigine 84371-65-3, Mifepristone 84449-90-1, Raloxifene 84625-61-6, Itraconazole 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 86541-75-5, Benazepril 87679-37-6, Trandolapril 88150-42-9, Amlodipine 88669-04-9, Trospectomycin 89778-26-7, Toremifene 89987-06-4, Tiludronate 90357-06-5, Bicalutamide 91161-71-6, Terbinafine 93390-81-9, Fosphenytoin 93413-69-5, Venlafaxine 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 94749-08-3, Salmeterol xinafoate 95233-18-4, Atovaquone 97240-79-4, Topiramate 97322-87-7, Troglitazone 97682-44-5, Irinotecan 98079-51-7, Lomefloxacin 98319-26-7, Finasteride 100986-85-4, Levofloxacin 101828-21-1, Butenafine 103577-45-3, Lansoprazole 103628-46-2, Sumatriptan 104227-87-4, Famciclovir 104987-11-3, Tacrolimus 105462-24-6, Risedronic acid 106133-20-4, Tamsulosin 106392-12-5, Oxirane, polymer with methyloxirane, block 106650-56-0, Sibutramine 106819-53-8, Doxacurium chloride 106861-44-3, Mivacurium chloride 107648-80-6, Cefepime hydrochloride 107753-78-6, Zafirlukast 109319-16-6, Factor VIII 110871-86-8, Sparfloxacin 111025-46-8, Pioglitazone 111406-87-2, Zileuton 112965-21-6, Calcipotriene 113427-24-0 113665-84-2, Clopidogrel 113852-37-2, Cidofovir 115103-54-3, Tiagabine 116094-23-6, Insulin aspart 117976-89-3, Rabeprazole 118072-93-8, Zoledronate 118292-40-3, Tazarotene 119914-60-2, Grepafloxacin 120014-06-4, Donepezil 121368-58-9, Olpadronate 121679-13-8, Naratriptan 122320-73-4, Rosiglitazone 123948-87-8, Topotecan 124832-26-4, Valaciclovir 127759-89-1, Lobucavir 127779-20-8, Saquinavir 129497-78-5, Verteporfin **131918-61-1**, Paricalcitol 133040-01-4, Eprosartan 133107-64-9, Insulin lispro 134523-00-5, Atorvastatin 134678-17-4, Lamivudine 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 139110-80-8, Zanamivir 139264-17-8, Zolmitriptan 139481-59-7, Candesartan 139639-23-9, Tissue type plasminogen activator 142128-59-4, Terzolin 143003-46-7, Alglucerase 143011-72-7, Granulocyte colony stimulating factor 143831-71-4 144034-80-0, Rizatriptan 144494-65-5, Tirofiban 144701-48-4, Telmisartan 145599-86-6, Cerivastatin 145941-26-0, Oprelvekin 146961-76-4, Alatrofloxacin 147059-72-1, Trovafloxacin 148553-50-8, Pregabalin 151126-32-8, Pramlintide 153559-49-0, Targretin 154361-50-9, Capecitabine 154598-52-4, Efavirenz 155213-67-5, Ritonavir 157810-81-6, Indinavir sulfate 158747-02-5, Frovatriptan 158966-92-8, Montelukast 159989-64-7, Nelfinavir 160337-95-1, Insulin glargine 162011-90-7, Rofecoxib 165101-51-9, Becaplermin 169148-63-4, Insulin detemir 169590-42-5, Celecoxib 171599-83-0, Sildenafil citrate 173146-27-5, Denileukin diftitox 191588-94-0, TNK-tPA

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid carriers for improved delivery of active ingredients in pharmaceutical compns.)

L9 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB Pharmaceutical oil-in-water emulsions for delivery of polyfunctional active ingredients with improved loading capacity, enhanced stability, and reduced irritation and local toxicity are described. Emulsions include an aqueous phase, an oil phase comprising a structured triglyceride, and an emulsifier. The structured triglyceride of the oil phase is substantially free of triglycerides having three medium chain (C6-C12) fatty acid moieties, or a combination of a long chain triglyceride and a polarity-enhancing polarity modifier. The present invention also provides methods of treating an animal with a polyfunctional active ingredient, using dosage forms of the pharmaceutical emulsions. For example, an emulsion was prepared, with cyclosporin A as the polyfunctional active ingredient dissolved in an oil phase including a structured triglyceride (Captex 810D) and a long chain triglyceride (safflower oil). The composition contained (by weight) cyclosporin A 1.0, Captex 810D 5.0, safflower oil 5.0, BHT 0.02, egg phospholipid 2.4, dimyristoylphosphatidyl glycerol 0.2, glycerol 2.25, EDTA 0.01, and water up to 100%, resp.

2001:300514 Document Number 134:331617 Oil-in-water emulsion compositions for polyfunctional active ingredients. Chen, Feng-jing; Patel, Mahesh V. (Lipocine, Inc., USA). PCT Int. Appl. WO 2001028555 A1 20010426, 82 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US28835 20001018. PRIORITY: US 1999-420159 19991018.

IT Acids, biological studies
Bases, biological studies
Bile acids
Bile salts
Canola oil
Carbohydrates, biological studies
Carotenes, biological studies
Castor oil
Ceramides
Coconut oil
Corn oil
Cottonseed oil
Enkephalins
Fatty acids, biological studies
Glycerides, biological studies
Glycolipids
Interleukin 2
Interleukin 3
Linseed oil
Lipoproteins
Lysophospholipids
Monoglycerides
Olive oil
Palm kernel oil
Palm oil
Peanut oil
Phosphatidic acids
Phosphatidylcholines, biological studies

Phosphatidylethanolamines, biological studies
Phosphatidylglycerols
Phosphatidylinositols
Phosphatidylserines
Phospholipids, biological studies
Polymers, biological studies
Polyoxyalkylenes, biological studies
Rape oil
Safflower oil
Soybean oil
Sphingomyelins
Sphingosines
Sunflower oil
Trace elements, biological studies
Tumor necrosis factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oil-in-water emulsion compns. for polyfunctional active ingredients)

IT 59865-13-3, Cyclosporin A 60142-96-3, Gabapentin 61270-78-8, Cefonicid sodium 61361-72-6, Dimyristoylphosphatidyl glycerol 61379-65-5, Rifapentine 61489-71-2, Menotropin 61869-08-7, Paroxetine 62013-04-1, Dirithromycin 62356-64-3 62893-19-0, Cefoperazone 63527-52-6, Cefotaxime 63585-09-1, Foscarnet sodium 63590-64-7, Terazosin 63612-50-0, Nilutamide 63675-72-9, Nisoldipine 64228-81-5, Atracurium besylate 64544-07-6, Cefuroxime axetil 65271-80-9, Mitoxantrone 65277-42-1, Ketoconazole 66376-36-1, Alendronate 66419-50-9, Bovine growth hormone 68099-86-5, Bepridil hydrochloride 68401-81-0, Ceftizoxime 68506-86-5, Vigabatrin 69049-74-7, Nedocromil sodium 69655-05-6, Didanosine 69756-53-2, Halofantrine 70288-86-7, Ivermectin 70458-92-3, Pefloxacin 70458-96-7, Norfloxacin 71486-22-1, Vinorelbine 72432-03-2, Miglitol 72559-06-9, Rifabutine 73384-59-5, Ceftriaxone 73590-58-6, Omeprazole 73963-72-1, Cilostazol 74011-58-8, Enoxacin 74103-06-3, Ketorolac 74356-00-6, Cefotetan disodium 74381-53-6, Leuprolide acetate 75706-12-6, Leflunomide 76420-72-9, Enalaprilat 76470-66-1, Loracarbef 76547-98-3, Lisinopril 76824-35-6, Famotidine 76963-41-2, Nizatidine 78110-38-0, Aztreonam 79350-37-1, Cefixime 79517-01-4, Octreotide acetate 79617-96-2, Sertraline 79794-75-5, Loratadine 79902-63-9, Simvastatin 81093-37-0, Pravastatin 81098-60-4, Cisapride 81103-11-9, Clarithromycin 81161-17-3, Esmolol hydrochloride 82410-32-0, Ganciclovir 82419-36-1, Ofloxacin 82626-48-0, Zolpidem 82952-64-5, Trimetrexate glucuronate 83799-24-0, Fexofenadine 83869-56-1, Granulocyte-macrophage colony stimulating factor 83881-51-0, Cetirizine 83905-01-5, Azithromycin 84057-84-1, Lamotrigine 84371-65-3, Mifepristone 84449-90-1, Raloxifene 84625-61-6, Itraconazole 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 86541-75-5, Benazepril 87679-37-6, Trandolapril 88669-04-9, Trospectomycin 89778-26-7, Toremifene 89987-06-4, Tiludronate 90357-06-5, Bicalutamide 91161-71-6, Terbinafine 93390-81-9, Fosphenytoin 93413-69-5, Venlafaxine 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 94749-08-3, Salmeterol xinafoate 95233-18-4, Atovaquone 97240-79-4, Topiramate 97322-87-7, Troglitazone 97682-44-5, Irinotecan 98079-51-7, Lomefloxacin 98319-26-7, Finasteride 100986-85-4, Levofloxacin 101828-21-1, Butenafine 103577-45-3, Lansoprazole 103628-46-2, Sumatriptan 104227-87-4, Famciclovir 104987-11-3, Tacrolimus 105462-24-6, Risedronic acid 106133-20-4, Tamsulosin 106650-56-0, Sibutramine 106819-53-8, Doxacurium chloride 106861-44-3, Mivacurium chloride 107648-80-6, Cefepime hydrochloride 107753-78-6,

Zafirlukast 110871-86-8, Sparfloxacin 111025-46-8, Pioglitazone 111406-87-2, Zileuton 112965-21-6, Calcipotriene 113189-02-9, Antihemophilic factor 113665-84-2, Clopidogrel 113852-37-2, Cidofovir 115103-54-3, Tiagabine 116094-23-6, Insulin aspart 117976-89-3, Rabeprazole 118072-93-8, Zoledronate 118292-40-3, Tazarotene 119914-60-2, Grepafloxacin 120014-06-4, Donepezil 121368-58-9, Olpadronate 121679-13-8, Naratriptan 122320-73-4, Rosiglitazone 123948-87-8, Topotecan 124832-26-4, Valaciclovir 127759-89-1, Lobucavir 127779-20-8, Saquinavir 129497-78-5, Verteporfin **131918-61-1**, Paricalcitol 133040-01-4, Eprosartan 133107-64-9, Insulin lispro 134523-00-5, Atorvastatin 134678-17-4, Lamivudine 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 139110-80-8, Zanamivir 139264-17-8, Zolmitriptan 139481-59-7, Candesartan 139639-23-9, Tissue type plasminogen activator 143003-46-7, Alglucerase 143011-72-7, Granulocyte colony stimulating factor 144034-80-0, Rizatriptan 144494-65-5, Tirofiban 144701-48-4, Telmisartan 145599-86-6, Cerivastatin 145941-26-0, Oprelvekin 146961-76-4, Alatrofloxacin 147059-72-1, Trovafloxacin 148553-50-8, Pregabalin 151126-32-8, Pramlintide 153559-49-0, Targretin 154361-50-9, Capecitabine 154598-52-4, Efavirenz 155213-67-5, Ritonavir 156259-68-6, Capmul MCM 157810-81-6, Indinavir sulfate 158747-02-5, Frovatriptan 158966-92-8, Montelukast 159989-64-7, Nelfinavir 160337-95-1, Insulin glargine 162011-90-7, Rofecoxib 165101-51-9, Becaplermin 169148-63-4, Insulin detemir 169590-42-5, Celecoxib 173146-27-5, Denileukin diftitox 191588-94-0, TNK-tPA 208666-87-9, Captex 810D
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oil-in-water emulsion compns. for polyfunctional active ingredients)

L9 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN
AB Drugs, especially low aqueous solubility drugs, are provided in a porous matrix form, preferably microparticles, which enhances dissoln. of the drug in aqueous media. The drug matrixes preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aqueous solubility, in a volatile solvent to form a drug solution, (ii) combining at least one pore forming agent with the drug solution to form an emulsion, suspension, or second solns., and (iii) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second solution to yield the porous matrix of drug. The pore forming agent can be either a volatile liquid that is immiscible with the drug solvent or a volatile solid compound, preferably a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has a faster rate of dissoln. following administration to a patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aqueous medium and administered parenterally, or processed using standard techniques into tablets or capsules for oral administration. Paclitaxel or docetaxel can be provided in a porous matrix form, which allows the drug to be formulated without solubilizing agents and administered as a bolus. For example, a nifedipine-loaded organic solution was prepared by dissolving 9.09 g of PEG 3350, 2.27 g of nifedipine, and 0.009 g of lecithin in 182 mL of methylene chloride. An aqueous solution was prepared by dissolving 3.27 g of NH4HCO3 and 0.91 g of PEG 3350 in 1.82 mL of water. The aqueous and organic solns. were homogenized and resulting emulsion

was spray dried. A suspension of the porous nifedipine drug matrix was prepared in 5% dextrose solution at a concentration of 2.5 mg/mL. A bolus injection of the suspension was tolerated when administrated to dogs.

2000:861473 Document Number 134:32972 Porous drug matrixes containing polymers and sugars and methods of their manufacture. Straub, Julie; Bernstein, Howard; Chickering, Donald E., III; Khatak, Sarwat; Randall, Greg (Acusphere, Inc., USA). PCT Int. Appl. WO 2000072827 A2 20001207, 45 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US14578 20000525. PRIORITY: US 1999-PV136323 19990527; US 1999-PV158659 19991008; US 1999-433486 19991104; US 2000-PV186310 20000302.

IT Artery
Bone
Eye
Heart
Lung
Mucous membrane
Neoplasm
Skin
Synovial fluid
(administration to; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT 50-28-2, Estradiol, biological studies 50-35-1, Thalidomide 50-99-7, Dextrose, biological studies 52-53-9, Verapamil 53-03-2, Prednisone 55-98-1, Busulfan 57-63-6, Ethinyl estradiol 58-61-7, Adenosine, biological studies 59-92-7, Levodopa, biological studies 67-78-7 67-97-0, Vitamin D3 67-97-0D, Vitamin D3, analogs 71-58-9, Medroxyprogesterone acetate 75-64-9, Erbumine, biological studies 77-36-1, Chlorthalidone 89-57-6, Mesalamine 126-07-8, Griseofulvin 128-13-2, Ursodiol 298-46-4, Carbamazepine 302-79-4, Tretinoin 321-64-2, Tacrine 363-24-6, Dinoprostone 437-38-7, Fentanyl 439-14-5, Diazepam 443-48-1, Metronidazole 518-28-5, Podofilox 745-65-3, Alprostadil 846-49-1, Lorazepam 1951-25-3, Amiodarone 3239-44-9, Dexfenfluramine 4759-48-2, Isotretinoin 5534-09-8, Beclomethasone dipropionate 5593-20-4, Betamethasone dipropionate 9002-68-0, Follitropin 9002-72-6, Growth hormone 9007-12-9, Calcitonin 9041-93-4, Bleomycin sulfate 10238-21-8, Glyburide 11096-26-7, Erythropoietin 12629-01-5, Somatropin 12633-72-6, Amphotericin 13311-84-7, Flutamide 15307-79-6, Diclofenac sodium 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 18559-94-9, Albuterol 20830-75-5, Digoxin 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 22204-53-1, Naproxen 27203-92-5, Tramadol 28860-95-9, Carbidopa 28981-97-7, Alprazolam 29094-61-9, Glipizide 30516-87-1, Zidovudine 32986-56-4, Tobramycin 33069-62-4, Paclitaxel 34911-55-2, Bupropion 36505-84-7, Buspirone 40391-99-9 41340-25-4, Etodolac 41575-94-4, Carboplatin 42399-41-7, Diltiazem 42924-53-8, Nabumetone 51022-70-9, Albuterol sulfate 51333-22-3, Budesonide 51773-92-3, Mefloquine hydrochloride 54143-55-4, Flecainide 54527-84-3, Nicardipine hydrochloride 54910-89-3, Fluoxetine 54965-21-8, Albendazole 54965-24-1, Tamoxifen citrate 55268-75-2, Cefuroxime 56124-62-0, Valrubicin 56180-94-0,

Acarbose 59729-33-8, Citalopram 60142-96-3, Gabapentin 60205-81-4, Ipratropium 63659-18-7, Betaxolol 65277-42-1, Ketoconazole 66085-59-4, Nimodipine 66376-36-1, Alendronate 66852-54-8, Halobetasol propionate 69655-05-6, Didanosine 70476-82-3, Mitoxantrone hydrochloride 72432-03-2, Miglitol 72509-76-3, Felodipine 72558-82-8, Ceftazidime 72956-09-3, Carvedilol 73384-59-5, Ceftriaxone 73590-58-6, Omeprazole 75330-75-5, Lovastatin 75695-93-1, Isradipine 75847-73-3, Enalapril 76095-16-4, Enalapril maleate 76547-98-3, Lisinopril 76824-35-6, Famotidine 76963-41-2, Nizatidine 77883-43-3, Doxazosin mesylate 78246-49-8, Paroxetine hydrochloride 78628-80-5, Terbinafine hydrochloride 78755-81-4, Flumazenil 79517-01-4, Octreotide acetate 79559-97-0, Sertraline hydrochloride 79794-75-5, Loratadine 79902-63-9, Simvastatin 80274-67-5, Metoprolol fumarate 81098-60-4, Cisapride 81103-11-9, Clarithromycin 82410-32-0, Ganciclovir 82752-99-6, Nefazodone hydrochloride 82834-16-0, Perindopril 83799-24-0, Fexofenadine 83905-01-5, Azithromycin 83919-23-7, Mometasone furoate 84625-61-6, Itraconazole 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 86541-74-4, Benazepril hydrochloride 86541-75-5, Benazepril 87679-37-6, Trandolapril 89778-27-8, Toremifene citrate 91161-71-6, Terbinafine 91421-42-0, Rubitecan 93413-69-5, Venlafaxine 93957-54-1, Fluvastatin 95058-81-4, Gemcitabine 95233-18-4, Atovaquone 97048-13-0, Urofollitropin 97322-87-7, Troglitazone 98048-97-6, Fosinopril 98079-52-8, Lomefloxacin hydrochloride 98319-26-7, Finasteride 99011-02-6, Imiquimod 99294-93-6, Zolpidem tartrate 100286-90-6, Irinotecan hydrochloride 100986-85-4, Levofloxacin 103577-45-3, Lansoprazole 103628-48-4, Sumatriptan succinate 103775-10-6, Moexipril 104227-87-4, Famciclovir 104632-25-9, Pramipexole dihydrochloride 106266-06-2, Risperidone 106463-17-6, Tamsulosin hydrochloride 106685-40-9, Adapalene 107753-78-6, Zafirlukast 109889-09-0, Granisetron 110871-86-8, Sparfloxacin 111470-99-6, Amlodipine besylate 111974-72-2, Quetiapine fumarate 112809-51-5, Letrozole 113806-05-6, Olopatadine 114798-26-4, Losartan 114977-28-5, Docetaxel 115956-12-2, Dolasetron 120014-06-4, Donepezil 124832-26-4, Valacyclovir 127779-20-8, Saquinavir **131918-61-1**, Paricalcitol 132539-06-1, Olanzapine 134308-13-7, Tolcapone 134678-17-4, Lamivudine 137862-53-4, Valsartan 140678-14-4, Mangafodipir trisodium 142373-60-2, Tirofiban hydrochloride 143011-72-7, Granulocyte colony-stimulating factor 144701-48-4, Telmisartan 145040-37-5, Candesartan cilexetil 147059-72-1, Trovafloxacin 147245-92-9, Glatiramer acetate 150378-17-9, Indinavir 154248-97-2, Imiglucerase 154598-52-4, Efavirenz 155141-29-0, Rosiglitazone maleate 155213-67-5, Ritonavir 158966-92-8, Montelukast 159989-65-8, Nelfinavir mesylate 161814-49-9, Amprenavir 162011-90-7, Rofecoxib 169590-42-5, Celecoxib 171599-83-0, Sildenafil citrate 679809-58-6, Enoxaparin sodium
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of porous matrixes containing hydrophilic polymers and sugars for
enhancement of drug dissoln.)

L9 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN
AB Prostate **cancer** cells contain specific receptors [vitamin D receptors (VDRs)] for 1α,25-dihydroxyvitamin D3 (1α,25(OH)2D3), which is known to inhibit the proliferation and invasiveness of these cells. These findings support the use of 1α,25(OH)2D3 for prostate **cancer** therapy. However,

because 1α,25(OH)2D3 can cause hypercalcemia, analogs of 1α,25(OH)2D3 that are less calcemic but that exhibit potent antiproliferative activity would be attractive as therapeutic agents. The authors investigated the effects of two different types of less calcemic vitamin D compds., 25-hydroxyvitamin D3 [25(OH)D3] and 19-nor-1α,25-dihydroxyvitamin D2 [19-nor-1,25(OH)2D2], and compared their activity to 1α,25(OH)2D3 on (a) the proliferation of primary cultures and cell lines of human prostate **cancer** cells; and (b) the transactivation of the VDRs in the androgen-insensitive PC-3 **cancer** cell line stably transfected with VDR (PC-3/VDR). 19-Nor-1α,25(OH)2D2, an analog of 1α,25(OH)2D3 that was originally developed for the treatment of parathyroid disease, has been shown to be less calcemic than 1α,25(OH)2D3 in clin. trials. Addnl., the authors recently showed that human prostate cells in primary culture possess 25(OH)D3-1α-hydroxylase, an enzyme that hydroxylates the inactive prohormone, 25(OH)D3, to the active hormone, 1α,25(OH)2D3, intracellularly. The authors reasoned that the hormone that is formed intracellularly would inhibit prostate cell proliferation in an autocrine fashion. The authors found that 1α,25(OH)2D3 and 19-nor-1α,25(OH)2D2 caused similar dose-dependent inhibition in the cell lines and primary cultures in the [3H]thymidine incorporation assay and that both compds. were significantly more active in the primary cultures than in LNCaP cells. Likewise, 25(OH)D3 had inhibitory effects comparable to those of 1α,25(OH)2D3 in the primary cultures. In the chloramphenicol acetyltransferase (CAT) reporter gene transactivation assay in PC-3/VDR cells, 1α,25(OH)2D3 and 19-nor-1α,25(OH)2D2 caused similar increases in CAT activity between 10-11 and 10-9 M. Incubation of PC-3/VDR cells with 5 + 10-8 M 25(OH)D3 induced a 29-fold increase in CAT activity, similar to that induced by 10-8 M 1α,25(OH)2D3. In conclusion, the authors' data indicate that 25(OH)D3 and 19-nor-1α,25(OH)2D2 represent two different solns. to the problem of hypercalcemia associated with vitamin D-based therapies: 25(OH)D3 requires the presence of 1α-hydroxylase, whereas 19-nor-1α,25(OH)2D2 does not. Both drugs are approved for human use and may be good candidates for human clin. trials in prostate **cancer**.

2000:242975 Document Number 133:13092 The in vitro evaluation of 25-hydroxyvitamin D3 and 19-nor-1α,25-dihydroxyvitamin D2 as therapeutic agents for prostate **cancer**. Chen, Tai C.; Schwartz, Gary G.; Burnstein, Kerry L.; Lokeshwar, Bal L.; Holick, Michael F. (Vitamin D, Skin and Bone Research Laboratory and Endocrine Section, Boston University Medical Center, Boston, MA, 02118, USA). Clinical Cancer Research, 6(3), 901-908 (English) 2000. CODEN: CCREF4. ISSN: 1078-0432. Publisher: American Association for Cancer Research.

TI The in vitro evaluation of 25-hydroxyvitamin D3 and 19-nor-1α,25-dihydroxyvitamin D2 as therapeutic agents for prostate **cancer**

AB Prostate **cancer** cells contain specific receptors [vitamin D receptors (VDRs)] for 1α,25-dihydroxyvitamin D3 (1α,25(OH)2D3), which is known to inhibit the proliferation and invasiveness of these cells. These findings support the use of 1α,25(OH)2D3 for prostate **cancer** therapy. However, because 1α,25(OH)2D3 can cause hypercalcemia, analogs of 1α,25(OH)2D3 that are less calcemic but that exhibit potent antiproliferative activity. . . [19-nor-1,25(OH)2D2], and compared their activity to 1α,25(OH)2D3 on (a) the proliferation of primary cultures and cell lines of human prostate **cancer** cells; and (b) the transactivation of the VDRs in the androgen-insensitive PC-3

cancer cell line stably transfected with VDR (PC-3/VDR). 19-Nor-1α,25(OH)2D2, an analog of 1α,25(OH)2D3 that was originally developed for the treatment of. . . does not. Both drugs are approved for human use and may be good candidates for human clin. trials in prostate **cancer**.

IT Vitamin D receptors
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(1,25-dihydroxyvitamin D3 analogs effect on prostate **cancer** cell proliferation and receptor transactivation in vitro)

IT Prostate gland
Prostate gland
(**neoplasm**, inhibitors; 1,25-dihydroxyvitamin D3 analogs effect on prostate **cancer** cell proliferation and receptor transactivation in vitro)

IT Antitumor agents
(prostate gland; 1,25-dihydroxyvitamin D3 analogs effect on prostate **cancer** cell proliferation and receptor transactivation in vitro)

IT 19356-17-3, 25-Hydroxyvitamin D3 32222-06-3, Calcitriol **131918-61-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(1,25-dihydroxyvitamin D3 analogs effect on prostate **cancer** cell proliferation and receptor transactivation in vitro)

IT 9081-36-1, 25-Hydroxyvitamin D3-1α-hydroxylase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(1,25-dihydroxyvitamin D3 analogs effect on prostate **cancer** cell proliferation and receptor transactivation in vitro)

L9 ANSWER 20 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB Vitamin Ds have been reported to have diverse effects on cell homeostasis, leading to suggestions that they have therapeutic applications extending beyond their traditional actions on the Ca2+/parathyroid/bone axis. As some of these potential indications carry an inherent risk of acute renal failure (ARF; e.g., **cancer** chemotherapy and organ transplantation), the goal of this study was to assess whether vitamin Ds directly affect renal tubule injury responses. Cultured human proximal tubular (HK-2) cells were exposed to physiol. or pharmacol. doses of either calcitriol (D3) or a synthetic vitamin D2 analog (19-nor) for 3 to 48 h. Their impact on cell integrity (percent lactate dehydrogenase (LDH) release and tetrazolium dye MTT uptake) under basal conditions and during superimposed injuries (ATP depletion/Ca2+ ionophore or iron-mediated oxidant stress) were determined As vitamin Ds can be anti-proliferative, cell outgrowth ([3H]thymidine uptake and crystal violet staining) was also tested. Finally, the action of D3 on in vivo ARF (glycerol-induced myoglobinuria) and isolated proximal tubule injury responses were assessed. D3 induced a rapid, dose-dependent increase in HK-2 susceptibility to both ATP-depletion/Ca2+-ionophore-and Fe-mediated attack without independently affecting cell integrity or proliferative responses. In contrast, D2 neg. affected only Fe toxicity and only after relatively prolonged exposure (48 h). D3 dramatically potentiated in vivo ARF (two- to three-fold increase in azotemia), suggesting potential in vivo relevance of the above HK-2 cell results. Proximal tubules, isolated from these glycerol-exposed mice, suggested that D3 can worsen tubule injury

despite a paradoxic suppression of H2O2 production In contrast, D3 had a mild neg. impact on cellular energetics (depressed ATP/ADP ratios), and it accentuated plasma membrane phospholipid breakdown. The latter was observed in both glycerol-treated and control tubules, suggesting a primary role in the injury-potentiating effect of D3. Vitamins D(s) may directly, and differentially, increase proximal tubule cell susceptibility to superimposed attack. This property should be considered as new uses for these agents are defined.

1999:395866 Document Number 131:194784 Calcitriol directly sensitizes renal tubular cells to ATP-depletion- and iron-mediated attack. Zager, Richard A. (Fred Hutchinson Cancer Research Center and the University of Washington, Seattle, WA, 98109-1024, USA). American Journal of Pathology, 154(6), 1899-1909 (English) 1999. CODEN: AJPAA4. ISSN: 0002-9440. Publisher: American Society for Investigative Pathology.

AB . . . on the Ca2+/parathyroid/bone axis. As some of these potential indications carry an inherent risk of acute renal failure (ARF; e.g., **cancer** chemotherapy and organ transplantation), the goal of this study was to assess whether vitamin Ds directly affect renal tubule injury. . .

IT **131918-61-1**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (vitamin D2 analog sensitizes renal tubular cells to iron-mediated cellular damage)

L9 ANSWER 21 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN

AB A method of treating the multiple sclerosis symptoms of a multiple sclerosis patient comprises administering to a multiple sclerosis patient an amount of a vitamin D compound effective to reduce symptoms and observing a reduction in symptoms. The effect of 1,25-dihydroxyvitamin D3 and other compds. in an animal multiple sclerosis model (exptl. autoimmune encephalomyelitis) was determined, as was the effect of 1,25-dihydroxyvitamin D3 on Th1 cell development and cytokine gene expression.

1997:557635 Document Number 127:215206 Vitamin D compounds for multiple sclerosis treatment. Deluca, Hector F.; Hayes, Colleen E.; Cantorna, Margherita T. (Wisconsin Alumni Research Foundation, USA). PCT Int. Appl. WO 9729740 A1 19970821, 32 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US14253 19960905. PRIORITY: US 1996-600913 19960213.

IT Cytokines
Gene, animal
Interleukin 2
Interleukin 4
Tumor necrosis factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(dihydroxyvitamin D3 effect on Th1 cell development and cytokine gene activation)

IT 1406-16-2D, Vitamin D, derivs. 32511-63-0, 1,25-Dihydroxyvitamin D3 103656-37-7 **131918-61-1** 195051-26-4 195051-27-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(vitamin D compds. for multiple sclerosis treatment)

L9 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. include I [R4,R5 = H, D, or R4R5 = double or triple bond; R3,R13 = H, (protected) OH, F, D, alkyl; Z = H, (protected) OH; X,Y = H, hydroxy-protecting group; R1 = CF3, CD3, (CH2)qH (q = 1-5); R2 = CF3, CD3, (CH2)pH (p = 1-5), or R1R2 = (CH2)m (M = 2-5); n = 1-5], II (X1,Y1 = H, acyl, alkylsilyl, alkoxyalkyl; U = H, alkyl, hydroxyalkyl, etc.), and III (R2 = H, Me, Et, propyl; X2,Y2 = H, acyl, hydroxy-protecting group). The vitamin D derivs. of the invention inhibit replication of human immunodeficiency virus in human cells and are therefore useful for treatment of AIDS. The compds. are also useful for treating other lentivirus infections and attendant immune and infectious disorders. Preparation of selected compds. in described. The derivs. of the invention were also studied with regard to cell differentiation activity and Ca mobilization/transport. For example, cyclopentano-1,25-dihydroxy-vitamin D3 (IV) and cyclopentano-1,25-dihydroxy-22E-dehydro-vitamin D3 (V) increased intestinal Ca transport and bone Ca mobilization (serum Ca levels determined). IV and V were also more active than 1,25-dihydroxy-vitamin D3 in inducing differentiation of HL-60 **leukemic** cells, making them useful not only as Ca regulating agents but also in the treatment of **neoplastic** diseases, especially **leukemias**. Biol. activity of a variety of other vitamin D derivs. is given.

1991:464738 Document Number 115:64738 Use of vitamin D compounds to inhibit AIDS virus. Pauza, Charles David; Deftos, Leonard John; Deluca, Hector Floyd (Wisconsin Alumni Research Foundation, USA). PCT Int. Appl. WO 9103246 A1 19910321, 81 pp. DESIGNATED STATES: W: AU, BR, CA, JP, KR; RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, IT, LU, ML, MR, NL, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1990-US5134 19900910. PRIORITY: US 1989-405857 19890911; US 1990-579341 19900907.

AB . . . mobilization (serum Ca levels determined). IV and V were also more active than 1,25-dihydroxy-vitamin D3 in inducing differentiation of HL-60 **leukemic** cells, making them useful not only as Ca regulating agents but also in the treatment of **neoplastic** diseases, especially **leukemias**. Biol. activity of a variety of other vitamin D derivs. is given.

ST vitamin D deriv AIDS treatment; **leukemia** inhibitor vitamin D deriv; calcium regulation vitamin D deriv; lentivirus inhibition vitamin D deriv; human immunodeficiency virus vitamin D deriv

IT **Leukemia**
(cell of, differentiation of, vitamin D derivs. for)

IT 103732-08-7 105687-81-8 128312-74-3 135078-56-7
RL: BIOL (Biological study)
(calcium mobilization and **leukemic** cell line HL-60 differentiation stimulation activity of)

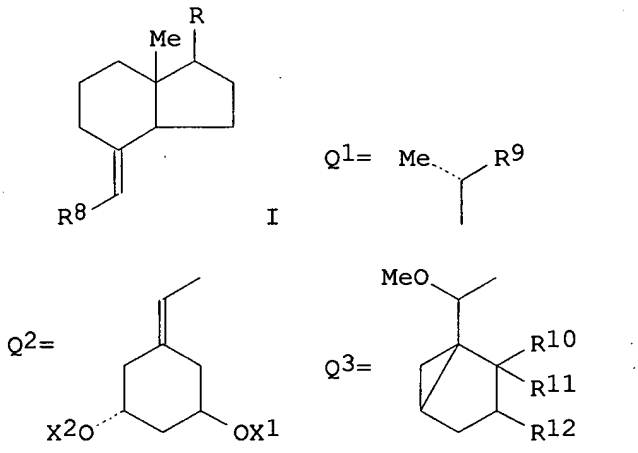
IT 32222-06-3 41294-56-8 103656-37-7 103656-40-2 108491-51-6
125448-38-6 128312-72-1 128312-76-5 130447-37-9 131918-60-0
131918-61-1 131918-62-2 132015-94-2 132015-95-3
135078-47-6 135078-48-7 135078-49-8 135078-50-1 135078-51-2

135078-52-3 135078-53-4 135078-54-5 135078-55-6 135111-94-3
RL: BIOL (Biological study)
(for AIDS treatment)

IT 19356-17-3 21343-40-8 54573-75-0 55721-11-4 56142-94-0
57333-95-6 57333-96-7 60133-18-8 65120-25-4 90191-28-9
97903-36-1 97903-37-2 103764-76-7 103764-86-9 107425-78-5
107425-86-5 110996-21-9 110996-22-0 110996-24-2 111024-90-9
111024-91-0 111024-92-1
RL: BIOL (Biological study)
(**leukemic** cell line HL-60 differentiation stimulation activity of)

IT 114694-09-6 123963-51-9 123963-52-0
RL: BIOL (Biological study)
(**leukemic** cell line HL-60 differentiation stimulation activity of, for AIDS treatment)

L9 ANSWER 23 OF 23 HCAPLUS COPYRIGHT 2005 ACS on STN
GI



AB The title compds. [I; R = H, (hydroxy)alkyl, fluoroalkyl, Q1; R8 = Q2; R9 = CHR7CHR6(CR4R5)nCR1R2R3; R1 = H, OH, acyloxy; R2, R3 = (hydroxy)alkyl, fluoroalkyl; R2R3 = (CH2)2-5; R4 = H, F, acyloxy, (hydroxy)alkyl, fluoroalkyl; R5 = R4, OH; R4R5 = O; R6, R7 = H, OH, acyloxy, F, alkyl; R6R7 = bond; n = 1-5; C-20, C-22, or C-23 may be replaced by O, S, or N] were prepared Thus, I [R = Q1, R9 = (CH2)3CMe2OH] (II; R8 = group Q3) (III; R10R11 = CH2, R12 = OH) was treated with OsO4 and the product with NaIO4 to give III (R10R11 = O, R12 = OAc) which was reduced in 2 steps to III (R10-R12 = H). The latter was stirred 20 min at 55° with HOAc to give, after deacetylation, II (R8 = Q2; X1 = X2 = H) which was as potent as 1α,25-dihydroxyvitamin D3 in promotion of differentiation of **leukemia** cells in vitro with no bone-calcification activity at 325.0 pmol/day for 7 days i.p. in rats.

1991:185853 Document Number 114:185853 Preparation of 19-norvitamin D derivatives as drugs. DeLuca, Hector F.; Schnoes, Heinrich K.; Perlman, Kato L.; Sicinski, Rafal R.; Prahl, Jean Martin (Wisconsin Alumni Research Foundation, USA). Eur. Pat. Appl. EP 387077 A1 19900912, 18 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL,

SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-302521 19900309.
PRIORITY: US 1989-321030 19890309; US 1990-481354 19900216.

AB . . . (R8 = Q2; X1 = X2 = H) which was as potent as 1α,25-dihydroxyvitamin D3 in promotion of differentiation of **leukemia** cells in vitro with no bone-calcification activity at 325.0 pmol/day for 7 days i.p. in rats.

IT **Neoplasm** inhibitors
(**leukemia**, norvitamin D derivs.)

IT 130447-37-9P 131918-60-0P **131918-61-1P** 131918-62-2P
132015-94-2P 132015-95-3P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as drug)

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